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THE BRITISH ENCYCLOPAEDIA OF MEDICAL PRACTICE

**INCLUDING
MEDICINE SURGERY
OBSTETRICS GYNAECOLOGY
AND OTHER SPECIAL SUBJECTS**

under the General Editorship of

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PUBLISHERS' ANNOUNCEMENT

Since the publication of the last Cumulative Supplement Sir Humphry Rolleston has died. We believe it to be in accordance with his wishes that we should refrain from eulogy. There is a simple epitaph, however, which will for all time remain in our publishing house 'The Rolleston Tradition survives'

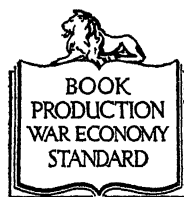
During the past year a very careful survey has been made of each subject in the *BRITISH ENCYCLOPAEDIA OF MEDICAL PRACTICE*. The customary referendum to the original authors had to be abandoned, instead, a special whole-time staff has been engaged on the work and when necessary advice has been sought from expert sources. In some cases the editorial commentaries of the Interim Supplement have been largely quoted, not only in fulfilment of the promise made to subscribers but also for the reason that from more than one we have had requests that such material be brought into the annual volumes.

The volume has been shortened, but much new matter has been added and the usual revision has been made, the Cumulative Supplement thus maintains its place as the complement of the twelve original volumes of the *Encyclopaedia*. The essential principle of selection is that information of doubtful authority or accuracy is not allowed within its pages, completely dissociated as they are from anything that is controversial or of doubtful or unproved value in Medicine. This explains why some subjects in the original *Encyclopaedia* have not been added to, on the other hand and for obvious reasons certain subjects have been given three, four or five pages.

This volume replaces previous Cumulative Supplements, and is therefore the current authentic addendum to the original *Encyclopaedia*.

BUTTERWORTH & Co (PUBLISHERS), LTD

January 1945



THE TYPOGRAPHY OF THIS BOOK CONFORMS
TO THE AUTHORIZED ECONOMY STANDARD

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CUMULATIVE SUPPLEMENT 1945

ABDOMINAL PAIN AND ACUTE ABDOMINAL EMERGENCIES

DIAGNOSTIC SIGNIFICANCE OF PAIN

Discarded theories of abdominal pain

Lewis and Kellgren return to the view of Lennander, long discarded by most authorities in Great Britain, that there is no true visceral pain, and that all the pain of visceral disease is essentially somatic in origin, or at any rate does not differ in its physiological mechanism from pain caused by simple stimulation of the mesentery. It is true that this conclusion is a little obscured by their insistence upon the pancreas as a source of motor reflexes in the abdominal wall when stimulated mechanically but, as has been pointed out, this phenomenon would seem to depend upon the inclusion of the pancreas within the mesentery of the cat's duodenum, and it would seem to be the nerves of the mesentery rather than of the pancreas that give rise to the reflex. The most significant finding in their experiments appears to be the complete absence of any such motor reflexes when the intestine itself is stimulated, either by pinching or by inflating a balloon within it.

1

Morley finds it difficult to accept their view that there is no true visceral pain apart from stimulation of somatic nerves in the mesentery or parietal peritoneum by abnormal peristalsis or inflammation of the gut. The condition of strangulated Richter's hernia, in which only a portion of the intestine on its anti-mesenteric border is involved, gives rise to severe spasms of colicky pain, as does the impaction of a large gall-stone in the small intestine. In neither of these conditions can it be supposed that there is any mechanical stimulation of somatic nerves in the mesentery. Further, if the view of Lewis and Kellgren were correct, there would be expected just as sure a reflex contraction of the rectus when a balloon is inflated in the duodenum as when the mesentery is pinched, whereas their experiments proved that this reflex never occurs in the balloon experiment. Morley therefore is convinced that their work does not disprove the existence of a true visceral pain, unassociated with any deep tenderness or hyperalgesia or reflex contraction of the muscles in the abdominal wall. Their experiments moreover go to prove the hypothesis, laid down by Morley in 1931, that a visceromotor reflex or viscerocutaneous radiation does not occur from the gastro-intestinal tract, and that the somatic manifestations in the abdominal wall that have been regarded by many, from Mackenzie onwards, as originating from the gastro-intestinal tract are really due to stimulation of deep-seated somatic nerves in the sensitive portion of the mesentery or the parietal peritoneum. These remarks apply to the gastro-intestinal tract only, and not to the urinary or cardiovascular systems.

Bentley and Smithwick in experiments on normal subjects found that balloon distension of the jejunum produced severe, colicky, nauseating pain in the upper abdomen, the area of distribution increasing with the severity of the pain. After division of the splanchnic and lower thoracic sympathetic chains on one side, balloon distension of the jejunum produced pain on the opposite side, and when both sides were deprived of their splanchnic and lower thoracic chains pain was not produced. In none of their experiments was there any cutaneous hyperalgesia, superficial or deep tenderness, or muscle rigidity observed. They regard other forms of visceral stimulation as sometimes responsible for such radiation and reflexes. The reason for this difference is obscure. They consider that visceral and somatic sensory fibres are in the same category, with a common anatomical basis which explains pain references and motor reflexes whether these arise from the abdomen, heart, or body surface. Further, they hold that the difference between somatic and visceral sensation is only one of degree.

The meaning of referred pain

Gunther and Reznick in discussing the relation of reno-ureteral disease to reflex abdominal pain state that the clinician should be able to determine the origin of the pain by a careful analysis of its distribution and the order of its evolution. There are 2 main patterns of abdominal pain, (1) pain which originates in the spinal nerve routes and is distributed according to the appropriate spinal segment and (2) the pain of visceral disease, the distribution of which does not strictly conform to segmental limits. The difficulty in settling the differential diagnosis arises because different viscera are supplied by nerves which come from identical spinal segments. In reno-ureteral disease the typical pain of renal colic may be experienced but there

- 1 are 4 additional reflexes, these being reno-gastric, reno-intestinal, reno-hepatic and reno-peritoneal. In reno-ureteral disease the pain tends to spread laterally and on the same side as that in which the affected organ is situated.

DIAGNOSIS OF ACUTE ABDOMINAL EMERGENCIES

- 2 Three hundred and seventy-five patients were treated, rightly or wrongly, for appendicitis by operation, 255 appendices removed were afterwards examined microscopically, and of these, 104 were not diseased, nevertheless the surgeons at the operation considered that 234 were abnormal. Temporary conditions such as obstruction by faecoliths or by kinking were the cause of pain. Females predominated in the group, most of the patients were aged from 10 to 19 years. The main symptom was pain and there had been previous attacks in 85 per cent of cases. There was nausea or vomiting or both in 64.8 per cent. A leucocytosis above 10,000 occurred in 16.6 per cent. There were no deaths. Willauer and O'Neill who reported the above findings state that after operation nearly 75 per cent of the patients had no complaints to make, there was discomfort or pain in 111 cases, and among the patients of this category there was a strong element of endocrine dysfunction.

Peritoneoscopy

Walker and Playfair describe endoscopic examination of the peritoneal cavity after inflation of air, termed peritoneoscopy, it is generally used for making a differential diagnosis or for determining operability in malignant disease, and may be undertaken in conjunction with biopsy as an alternative to laparotomy. General or spinal anaesthesia is required. Air is injected into the peritoneal cavity by means of a sterile needle and bellows, after inflation the needle is withdrawn, a trocar and sheath are inserted, and the telescope is passed down the sheath. After examination the air is allowed to escape and the sheath is withdrawn.

Clinical applications

Hamilton states that newer indications for peritoneoscopy include (1) the differential diagnosis of obstructive and other types of jaundice, (2) the differentiation of bleeding peptic ulcer and bleeding from an oesophageal varix, (3) the differential diagnosis of acute appendicitis and salpingitis, (4) the examination of gunshot and stab wounds of the abdomen, (5) the recognition of rupture of follicular ovarian cysts.

The use of the peritoneoscope is limited. Peritoneoscopy is clearly indicated in ascites of uncertain origin, there is no more danger here to the patient than there would be when paracentesis is performed. The method can also be used for investigating enlargement of the liver without any indication of the cause. With regard to the amount of air to be used in pneumoperitoneum, as a rule some 2 or 3 litres is necessary. Another important point is that air is the most satisfactory medium for use in peritoneoscopy. Normal saline has also been used.

Playfair, in summing up the value of the peritoneoscope, thinks that it is of value in the diagnosis of selected groups of cases and that it is satisfactory so far as the conducting of a biopsy is concerned. The fact that peritoneoscopy is safe means that it might yet be usefully employed for sterilization and observation of the progress of abdominal and pelvic disease.

- Bentley, F. H., and Smithwick, R. H. (1940) *Lancet*, 2, 389
Gunther, L., and Reznick, S. (1943) *Urol. cutan. Rev.*, 47, 6
Hamilton, J. E. (1941) *Amer. J. Surg.* N.S., 54, 668
Lewis, T., and Kellgren, J. H. (1939) *Clin. Sci.*, 4, 47
Morley, J. (1931) *Abdominal Pain*. Edinburgh
Playfair, P. L. (1943) *Proc. R. Soc. Med.*, 39, 450
Walker, R. M., and Playfair, P. L. (1942) *Lancet*, 1, 159
Willauer, G. J., and O'Neill, J. F. (1943) *Amer. J. med. Sci.*, 205, 334

ABORTION

NATURAL AND UNINTENTIONAL ABORTION

Preventive treatment

Progesterone

- 12 Browne, Henry and Venning interpret the rise in pregnanediol excretion which occurs from about the seventieth to the ninetieth day in most normal cases as being due to the beginning of secretion of progesterone by the placenta. It was previously thought that, since the corpus luteum in many cases degenerates about the third month, and since the ovaries could be removed and pregnancy continued, progesterone was unnecessary during the latter part of human pregnancy. The time at which the transition of function from ovary to placenta occurs varies in different individuals and in the same individual in different pregnancies. The authors believe that, if the corpus luteum ceases to produce progesterone for any length of time before the placenta begins to secrete it, abortion will follow. The time at which diminution of the corpus luteum hormone is most likely to occur is therefore during the transition period between the ovarian and placental phases, namely

during the late second and the third months, this is the critical period of pregnancy

The situation with regard to defective hormonal output and abortion is not yet stabilized and much useful work has been done by Hain, who is not prepared to agree that abortion is the result of hormonal deficiencies. In her investigations into cases of threatened abortion she found that the gonadotrophin and pregnanediol secretions were normal. She suggests that the production of hormones may be quite normal but that there may be improper use of the supply. Despite these conclusions it is clear that if progesterone is given in doses of from 5 to 10 milligrams thrice weekly, or chorionic gonadotrophin 100 rat units thrice weekly, the effects are very satisfactory in both threatened and habitual abortion.

CLINICAL ASPECTS OF ABORTION

Clinical varieties

General treatment

Holtz studied the results of different methods of treating abortion, in 2,718 cases, as carried out in 3 obstetrical clinics in Stockholm. He distinguished abortions occurring in the first 3 months of pregnancy, of which there were 1,583 cases, from abortions or premature births occurring in from the fourth to the seventh month. With regard to the first group Holtz states that in uncomplicated cases without severe haemorrhage both the immediate and the late results were better after active treatment consisting of prompt emptying of the uterus by means of Saenger's forceps and curettage. It was found that spread of infection occurred less often, that the mortality was lower, that the period during which the patient was confined to bed was of shorter duration, and that subsequent sterility was less frequent than after conservative treatment. In febrile cases the better results of active treatment were particularly noticeable. In a subsequent study of patients in this group, carried out at least 4 years after the abortion, it was found that conservative treatment was followed by sterility more frequently than active treatment was, and also that tubal pregnancy was more common after conservative treatment.

With regard to abortions occurring during the later months of pregnancy, in most cases both the foetus and the placenta were expelled spontaneously with or without the aid of oxytocics. The results of expectant treatment were good in both febrile and non-febrile cases. Only in cases with retention of the placenta did the need for active treatment arise, and in such cases conservative treatment gave rise to a higher morbidity and to a longer period spent in hospital. Further observation of this group 4 years or more after the abortion showed that active treatment in cases of retention of the placenta gave as good late results as conservative treatment in cases without retention of the placenta.

From this study it would appear that the treatment of cases of abortion during the first 3 months of pregnancy should be active, whereas, after the third month, treatment should be conservative, except in cases of retention of the placenta.

ARTIFICIAL AND INTENTIONAL ABORTION

Legal position of practitioner

The conclusions to be deduced from the case of *R. v. Bourne* which was tried at the Old Bailey on 19th July 1938 are as follows. To be legal the operation must be performed by a qualified medical man in good faith for the purpose only of saving the life of the woman, and 'saving the life' would seem to include 'preventing the patient from becoming a mental and physical wreck so that her life is endangered thereby'. If the surgeon is of opinion, on reasonable grounds and with adequate knowledge, that the probable consequence of a continuance of the pregnancy would be to make the woman a mental and physical wreck, the operation is apparently justifiable as an operation for the preservation of the mother's life, except in the case of a feeble-minded or 'prostitute-minded' woman. When an operation is justifiable on the grounds just stated, the surgeon is not required to wait until the woman is in peril of immediate death, but it is his duty to perform the operation without delay.

Browne, J. S. L., Henry, J. S., and Venning, E. H. (1939) *Amer. J. Obstet. Gynec.*, **38**, 927.

Hain, A. M. (1942) *J. Endocrinol.*, **3**, 10.

Holtz, F. (1938) *Acta obstet. gynec. scand.*, **18**, 245.

ABORTUS FEVER

TREATMENT

Several cases have been reported in which the use of sulphanilamide has given striking results in the treatment of undulant fever. Berger and Schnetz treated a patient with prontosil by mouth, Suchier employed prontosil rubrum, de Millas gave daily injections of prontosil soluble. In all 3 cases the temperature had fallen to normal within a week and relapse did not occur. Richardson also treated 2 cases, in the first patient the temperature fell after 6 days' treatment with prontosil album,

- 13 0.6 gramme twice daily, and an injection of 5 cubic centimetres of a 5 per cent solution of prontosil soluble on each of 4 consecutive days. In this case symptoms returned after 4 weeks and were relieved by prontosil treatment and further relapse has not since occurred. In the second case the patient's temperature fell after 4 days of treatment. Francis carried out some tests *in vitro* with the organisms recovered from one of his cases, the results of those tests appear to show that *Brucella abortus* was much more susceptible to the action of sulphanilamide *in vitro* than was the pyogenic streptococcus under the same conditions.

Berger, W., and Schnetz, H. (1937) *Med. Klinik*, **33**, 594.

Francis, A. E. (1938) *Lancet*, **1**, 496.

de Millas, W. (1937) *Der Landarzt*, **32**, 423.

Richardson, L. A. (1938) *Lancet*, **1**, 495.

Suchier, W. (1937) *Fortschr. Ther.*, **13**, 305.

ACANTHOSIS NIGRICANS

AETIOLOGY

- 14 The question whether or not the juvenile and adult cases should be regarded as examples of one and the same disease remains undetermined. Behdjiet, analysing a large number of cases of both types taken together, concluded that most cases were not attended by malignant developments and added the argument against a necessary malignant connexion that, in view of the frequency of cancer, the accompaniment of acanthosis should be more common than it is.

Several observers regard endocrine disturbance as a probable cause, thyroid, pituitary and gonads (Behdjiet), and adrenals (Gordon) being the glands more commonly affected. Dowling and Freudenthal reported a case with the most unusual accompaniment of tricho-epithelioma, and suggested that the same (unknown) change which produces the epidermal proliferation indicated by the term, acanthosis, also produces the epitheliomatous proliferation.

A juvenile case with remarkable familial history (mother, two maternal uncles, and maternal grandmother) is reported by Tolmach.

Behdjiet, H. (1932) *Bull. Soc. franç. Derm. Syph.*, **39**, 192.

Dowling, G. B., and Freudenthal, W. (1938) *Brit. J. Derm.*, **50**, 467.

Gordon, H. (1936) *Brit. J. Derm.*, **48**, 639.

Tolmach, J. A. (1939) *Arch. Derm. Syph., N.Y.*, **40**, 819.

ACCESSORY SINUSES OF THE NOSE

THE ACCESSORY SINUSES OF THE NOSE

Inflammatory diseases

Catarrhal inflammation

- 15 'Displacement' treatment is useful for catarrhal sinusitis in moderate or long-standing cases to promote drainage, especially of the ethmoidal cells. It was originally described by Proetz in 1931, and in 1939 Birdsall recorded successful results in children. The apparatus and technique are simple. The underlying principle is the introduction of some shrinking or other fluid into the sinuses by the application of alternating positive and negative pressures to the air in the nose and sinuses. The solution in general use is 0.5 per cent ephedrine in normal saline.

Birdsall, S. E. (1939) *J. Laryng.*, **54**, 549.

Proetz, A. W. (1931) *Displacement*. St. Louis.

ACHALASIA

IN THE ALIMENTARY TRACT

Of the cardiac sphincter

- 18 The diagrams in Vol. I on page 119 (Fig. 27) require modification as achalasia of

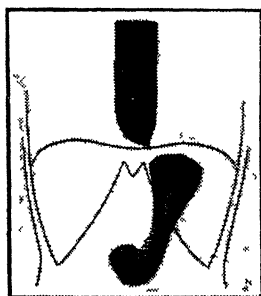


FIG 1—Achalasia of the cardia, showing absence of gastric air-bubble owing to lock formed by food and saliva permanently filling the lower six inches of the dilated oesophagus. (From the *British Medical Journal*, 1938.)

the cardia is the one condition in which there is not a gastric air-bubble. This is due to the fact that the food retained in the oesophagus completely blocks it and

prevents the air normally swallowed with food and drink from entering the stomach (see Fig 1)

Hurst, A (1938) *Brit med J*, 1, 661

ACNE

ACNE VULGARIS

Aetiology

Cohen concludes that acne is very frequently associated with certain endocrine disturbances such as tumours of the adrenal cortex and arrhenoblastoma, and occurs also during androgen administration. Otherwise there does not appear to be any definite association with endocrine disorders, although the development of acne at puberty and the menopause suggests a hormonal factor. Certain skin changes, such as Darier's keratosis, are probably necessary before acne can develop and these may be dependent on an endocrine imbalance. In cases in which an endocrine disturbance is obvious the appropriate treatment will also improve the acne but otherwise, so far as is yet known, endocrine treatment is not justified.

Stokes and Sternberg, on the basis of observations of 921 cases of acne over a period of 15 years, came to the following conclusions. The age of onset of the disease, the grade of involvement, and the prognosis are influenced by hereditary or familial considerations. The control of recognized hyperactivity of the sebaceous glands is still largely a matter of local treatment. The hypothesis of a double infection, and the close relation of acne to seborrhoea of the scalp, render essential thorough treatment of the scalp. Allergy, including sensitivity to foods (milk, chocolate), contributes many important elements in the behaviour of acne. A local infection-heightened process of sensitization appears to form part of the mechanism of extension and behaviour of acne under treatment. The contact inoculative factor is, in some cases, of major aetiological importance. It has a close relation to the psycho-neurogenic component. Fatigue and exhaustion, through their influence on resistance to infection, vasomotor instability, and the allergic state, play an important part in the behaviour of acne during school years and in causing relapse. Vitamin therapy, particularly with vitamin B complex in large doses, is useful.

Cohen, E L (1941) *Brit J Derm*, 53, 269

Stokes, J H, and Sternberg, T H (1939) *Arch Derm-Syph*, N Y, 40, 345

ACROMEGALY

PATHOLOGY

Grafflin mentions an unpublished thesis with illustrations of the normal, the acromegalic and the hyperplastic nephritic human nephron, as shown in reconstruction models made by Turley. In Turley's model of the nephron in acromegaly, taken from kidneys twice the normal size, the convoluted part of the proximal tubules was greatly increased in length, but the glomeruli were not enlarged as they were in the cases described by Cushing and Davidoff. In Turley's reconstructed model of chronic nephritis the outstanding feature was enormous enlargement of the proximal tubules, both pars convoluta and pars recta.

CLINICAL PICTURE

Changes in bone and other tissues

Radiological appearance of vertebral column

Chester and Chester report the radiological appearances of the vertebral column of patients with long-standing advanced acromegaly. The bodies of the vertebrae often show characteristic changes in the adjacent intervertebral disks, and in addition, a specific spondylitis, and an increase in the antero-posterior diameter of the bodies of the lower thoracic vertebrae. In the authors' cases the antero-posterior diameter of the bodies of the lower thoracic vertebrae exceeded that of the lumbar vertebrae. These changes are due to growth of new bone on the lateral and anterior aspects of the vertebral bodies. The margins of this partial bony growth are fissured so that a row of tooth-like processes appears above and below a vertebral disk. Sometimes the growth of bone at the diaphysis is more prominent peripherally than centrally. This gives rise to a spondylitis characterized by the symmetry of the spondylitic processes, and is regarded as specific for acromegaly. This spondylitis is more pronounced laterally than anteriorly. The spondylitis of acromegaly can readily be detected by the symmetry of the spondylitic processes. The growth of the intervertebral disk parallels that of the body of the vertebra, the new disk being laid down from the perichondrium. The new intervertebral disk is thinner than the old biconvex disk. Its margins are irregular, and new bone may even protrude into the intervertebral disk.

DIAGNOSIS

Differentiation from other changes of bone

Acropachydermia with pachyperiostitis

Brugsch describes a new condition, acropachydermia with pachyperiostitis, which includes cases of so-called pseudo-acromegaly, acromegalism, cutis verticis gyrata

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with acromegaly, pachyacria, megalia cutis et ossium, generalized hyperostosis and *pachydermie plicaturee avec pachyperostose des extrémités*. They represent the same abnormality of growth, with clubbing of the extremities, thickening of the skin of the face, scalp and extremities, and deformities of the long bones and their periosteum. The condition appears to have been noted only in males. The only two features common to acromegaly are overgrowth of the bones of the hands and feet and a tendency to sweat. Brugsch has collected about 32 cases of the disease. X-ray films of the sella turcica have been normal in most cases. The disease does not progress after the age of 25 years and does not endanger life. The causation is unknown.

TREATMENT

Use of hormones

Doses varying from 10,000 to 50,000 international units of oestrogen were given in a series of 4 cases reported by Hutton and Reiss, in which the chemical changes were most carefully observed and the excretion of gonadotrophic hormone and ketosteroid have been investigated. The use of hormones in acromegaly began in 1936 and subsequently there have been various other reports of its use, the action is such that large doses of oestrin will impair and partly suppress the functions of the anterior lobe of the pituitary gland, and will thus cause partial degeneration of the acidophil cells. Kirklin and Wilder adopted this treatment for 4 male and 4 female acromegalic patients, and the general outcome of the treatment was that 3 patients clearly improved, that headache was relieved in 4 out of the 6 cases, and that the size of the body generally was decreased, shoes and hats for instance becoming loose. So far as the visual fields were concerned, the results were disappointing.

In Hutton and Reiss's series 3 of the 4 cases showed well developed acromegaly, and the fourth patient had incipient signs. After treatment by oestrogens as mentioned above there was (1) decrease in size of the thickened phalangeal joints, (2) an extremely rapid improvement in the subjective symptoms such as headache, giddiness and amblyopia, and improvement in vision. The disadvantage associated with oestrogen treatment is that the great amount of oestrogen required affects the gonadal function, it has been suggested that gonadotrophic hormone might be used as a balancing drug.

Brugsch, H. G. (1941) *Arch intern Med*, **68**, 687

Chester, W., and Chester, E. M. (1940) *Amer J Roentgenol*, **44**, 552

Cushing, H., and Davidoff, L. M. (1927) *Monogr Rockefeller Inst med Res* No 22

Grafflin, A. L. (1939) *Arch Path*, **27**, 691

Hutton, E. L., and Reiss, M. (1942) *J ment Sci*, **88**, 550

Kirklin, D. L., and Wilder, R. M. (1936) *Proc Mayo Clin*, **11**, 121

ACTINOMYCOSIS

TREATMENT

Sulphonamide compounds

26

The value of sulphonamide compounds in the treatment of actinomycosis has been proved in more than one series of cases. Dobson, Holman and Cutting report complete cures of actinomycosis of the jaw, lungs, ribs and abdomen. Dorling and Eckhoff obtained complete recoveries in 80 per cent of patients treated, they used both sulphanilamide and sulphapyridine, singly or in combination.

Surgical

Results of radical treatment

So far as the surgical treatment of actinomycosis is concerned it is clear that early diagnosis is essential if the treatment is to have any success. This has been stressed by Randall who prefers above all other forms of treatment complete surgical eradication of the diseased area. This can be accomplished only if the condition is recognized in the early stages, therefore in all cases in which there is suppuration of an area in the head or neck region and which has lasted for not more than 2 weeks, the possibility of actinomycosis must not be forgotten. Randall has used this treatment fairly extensively and has had one death in 16 cases. It has been possible to keep under observation subsequently 12 patients and in these there has not been a relapse during a period which varies from 4 to 10 years. It is emphasized that one operation may not completely clear out all the diseased tissue, in such cases further surgical interference is necessary and may have success. The curette may be used but excision by diathermy has also proved successful. Radical surgical eradication of actinomycosis does not necessarily indicate that treatment by drugs is to be given up, on the contrary, it is pointed out that the giving of potassium iodide is a very useful adjuvant measure and X-ray therapy has also proved of the greatest assistance in the healing of the lesions. Actinomycosis of the head and neck is prognostically more favourable than actinomycosis in other parts of the body, this may be due to the

fact that in the neck and face the disease is more easily recognized and more accessible but there is no reason why successful surgical treatment of radical type should not be applied to lesions of the thorax and abdomen, again early diagnosis is the essential factor. The reason for failure in these regions is that patients delay too long before consulting the surgeon

Dobson, L., Holman, E., and Cutting, W (1941) *J Amer med Ass*,
116, 272

Dorling, G C., and Eckhoff, N L (1940) *Lancet*, 2, 707

Randall, O S (1942) *Amer J Surg NS*, 57, 433

ACTINOTHERAPY

ARTIFICIAL LIGHT TREATMENT

Physiology

Bactericidal power of ultra-violet rays

Air disinfection—A considerable amount of research has been done with regard to ultra-violet rays and destruction of bacteria, naturally there are several factors which influence the process but success has been achieved in the disinfection of air by ultra-violet rays. Wells states that the degree of disinfection is dependent upon the various organisms present, the humidity of the atmosphere, the state of bacterial suspension, the size of the room, the movement of the air and the quality, duration and uniformity of the radiation used. Tests are made to discover changes in density of bacteria, the reduction being calculated after a certain measured space has been radiated by allowing fresh air to enter the space and by taking a measurement of the number of bacteria then present. The difference in readings presumably indicates the bacterial irradiation. The degree of disinfection is proportional to the lethal irradiation intercepted by the living bacterial cells, it is found that in the middle ultra-violet section of the spectrum (2,000 to 3,000 Ångströms) the radiation waves are highly bactericidal. Bacteria are found to be more susceptible to ultra-violet waves when they are in dry air than when they are in suspension in water. Another very important factor is the distance of the bacteria from the source of radiation. It is most essential that the irradiation dose should be of uniform density, the greater the variations the less is the killing power of the waves.

Practical use of the above principles, for instance in children's hospitals, apparently reduces the incidence of infection. Del Mundo and McKhann reported experiments made with irradiation of the air in wards. In the winter of 1939-40, and in a non-irradiated ward, the infections reached a total of 12.5 per cent whereas in a ward in which the cubicles were protected in front and above by ultra-violet irradiation, the cross-infection amounted to 2.7 per cent only.

del Mundo, F., and McKhann, C F (1941) *Amer J Dis Child*,
61, 213

Wells, W F (1942) *Arch phys Ther*, 23, 143

ADENOIDS

DIAGNOSIS

Radiological methods

According to Calthrop if a soft ray is used to show up details of the soft tissues of the nasopharynx the presence of adenoids may be detected in children. The chin is raised and a true lateral view of the skull is taken. The best results are obtained when the central ray passes 1 inch below and in front of the external auditory meatus. Provided that the adenoid tissues have not been interfered with and that in effect they are complete, it is possible by the above method to demonstrate on the film an opaque mass at the site of the adenoid tissues in the nasopharynx.

TREATMENT

Use of X-rays

Radiotherapy has been used in the treatment of adenoids in infants and in children. Clement, Gilbert and Clenet in reporting their results point out that overgrowth of adenoid tissue is directly related to the state of the pituitary body and they further assert that because the lymphoid mass is reduced by a course of X-ray treatment and because also the hypersecretion of adenoids is thus inhibited the radiotherapy method is better than that of surgical removal. The method advised is as follows. The eyes of the patient are protected by lead-covered glasses and irradiation is carried out in the plane of the mandible. A second plane of irradiation takes in laterally the auricular and zygomatic regions. If irradiation on the above lines is not completely successful a third field is chosen with the rays centred on the nose. A distance of 28 centimetres is always maintained and screening is effected by using 0.5 millimetre of copper, 1 millimetre of aluminium and 1 centimetre of wood. From 360 r to 600 r were irradiated in each field in 3 sittings, this total varying according to the age of the patient and the signs and symptoms of the case. Good

results were reported in two-thirds of all cases and there were not any accidents or complications

Calthrop, G T (1940) *Lancet*, 1, 1005

Clement, R, Gilbert, P, and Clenet, E (1939) *Pr med*, 47, 786

ADRENAL GLAND DISEASES

ADRENAL HYPOPLASIA AND INSUFFICIENCY

Addison's disease

Treatment

- 30 *Desoxycorticosterone acetate*—There have not been any fundamental advances since the synthesis of desoxycorticosterone acetate was effected, but some knowledge of the use and limitations of the substance has been obtained and the various routes of administration have been investigated. Its influence on salt and water balance is great, and over-dosage results in oedema, even to the extent of general anasarca, hypertension and cardiac insufficiency (Ferrebee, Ragan, Atchley and Loeb, Ryan and McCullagh). The above complications are particularly likely to occur if, in addition to large doses of the hormone, large amounts of salt are taken. It is rare for complications to occur if extra salt is not taken, but even so they may ensue. As regards the dosage of desoxycorticosterone acetate, by the intramuscular route 5 milligrams daily is sufficient in a mild case, whereas a patient severely affected may require 20 milligrams. Some patients, however, appear to be hypersensitive as judged by local reactions, which may be so severe as to make continued therapy impossible.

(1) Intramuscular injection. For this purpose desoxycorticosterone acetate is prepared in ampoules of 1 cubic centimetre of arachis or sesame oil containing 5 milligrams of desoxycorticosterone acetate. Judging by clinical experience, Simpson^{1,2} found that 5 milligrams were equivalent to 10 cubic centimetres of cortin, but Wilkinson thought that the equivalent in cortin was nearer to 20 or even 30 cubic centimetres. As with cortin, the beneficial effect is noticed within an hour and persists for from 12 to 24 hours. Unfortunately in some patients severe local reactions occur at the site of injection and, apart from its inconvenience, therapy by this route soon ceases to be effective.

(2) Cutaneous inunction. For this method, 20 milligrams of desoxycorticosterone acetate are dissolved in a 1 cubic centimetre ampoule of alcoholic solution (100 milligrams of benzyl alcohol). The contents of an ampoule are rubbed into the skin of the thigh, abdomen or arm by the patient, the process taking from 10 to 20 minutes. It is an easy and effective route of administration and is quite painless, the only disadvantage is the relatively high cost, since the dose by this route is 4 times greater than that required by intramuscular injection. Initial reports were made by Simpson in 1939, and up to the present time this form of therapy has proved very satisfactory.

(3) Insertion of tablets under the skin. In 1937 Deanesly and Parkes showed that oestrone and testosterone tablets, when inserted under the skin of animals, were gradually absorbed over a period of months. In 1938 and 1939, Simpson used this technique for Addison's disease. Initially, 4 tablets of 50 milligrams each of desoxycorticosterone acetate were inserted into the subcutaneous fat of the abdomen under local anaesthesia. This dose proved sufficient for mild degrees of adrenal gland insufficiency, but for more severe degrees 6 tablets of 100 milligrams each were employed. The worst cases, even with such a dose, required supplementary therapy with salt, or injections of desoxycorticosterone acetate. Thorn, Howard and Emerson, working independently, used a similar technique in Addison's disease, basing their dosage on animal experiments. They suggested that for every 0.5 milligram of hormone in oil required daily by the intramuscular route, a tablet or pellet of 100–150 milligrams is required. Thus for a patient requiring 5 milligrams daily by injection, 10 or more tablets of 100 milligrams of desoxycorticosterone acetate should be inserted under the skin. As a patient severely ill with Addison's disease requires 20 milligrams daily by injection, 40 such tablets would be required. From clinical experience this estimate is too high, and the probable explanation is that with intramuscular injection a much greater proportion of the hormone is wasted by excretion. The duration of effect appears to vary between 3 and 8 months, this individual clinical variation is at least partly due to the amount of hormone absorbed in the later months being less than that absorbed in the earlier period. It is very important to remember that any conditions causing extra requirements of hormone, namely infection or special exertion, must be met by supplementary injections.

Further experience with the subcutaneous insertion of tablets of desoxycorticosterone acetate has proved the method to be efficacious over a period of 3 years, when repeated at intervals of 4 months. The tablets each weigh 50 or 75 milligrams and, if the daily injection dose required by the patient is 5 milligrams, approximately 500 milligrams subcutaneously are sufficient, if the daily dose is 10 milligrams, 800 milligrams are required, if the daily dose is 20 milligrams, 1,200

milligrams are required. These data are based on clinical experience and the doses are slightly lower than those advocated by Thorn, Howard and Emerson which were based on animal experiments, and which comprised 5 milligrams daily by injection, indicating an equivalent of 1,000 milligrams subcutaneously implanted. Simpson has not used more than 1,200 milligrams in any one case.

(4) Sublingual administration. Another route that has been used with success is the sublingual route. Turnoff and Rowntree found that 6 drops (1 milligram) of desoxycorticosterone acetate in propylene glycol, placed under the tongue 6 times daily and retained there for some 15 minutes before being expectorated, allowed sufficient absorption in 2 cases to maintain the patients in relatively good health. The effect was also evident from the fact that the addition of salt produced oedema. Simpson has used this method, and does not find it of practical application except in mild degrees of adrenal insufficiency.

Cortical extract—For convenience, it is advisable to refer to cortical extract as cortin, without, however, implying any particular extract. It is given by intramuscular injection, into the buttock or thigh. The dose in a mild case is about 5 cubic centimetres daily, and for severe insufficiency, 20 cubic centimetres daily, or more. During periods of infection, or in the course of surgical procedures, the quantity of cortin should be doubled or trebled. When the daily dose is large, cortin may be given twice daily. If there is some pain on injection, 0.5 cubic centimetre, or less, of 2 per cent novocain may be added to the cortin in the syringe. Persistent local reactions are unusual when cortin is given by the intramuscular route. Cortin may also be given intravenously, and usually does not cause any allergic reaction but, apart from the technical difficulty of daily intravenous injections, it has been shown that a refractory state develops after some weeks (Hartman, Lewis and Toby). This does not occur with intramuscular injections. Cortin is supplied in 10 cubic centimetre rubber-capped bottles, and retains its potency for some months if kept in a cold place.

HYPERFUNCTION OF THE ADRENAL MEDULLA

Symptoms

Phaeochromocytoma

Clinical picture—At various times within the period 1938–43 references have appeared in the literature with regard to phaeochromocytoma, these generally taking the form of case reports. The condition is briefly referred to in the *Encyclopaedia*, Vol I, p. 251. In amplification certain facts reported by McCullagh and Engel are to be noted. In each case there was the usual hypermetabolism depending upon the phaeochromocytoma. Paroxysmal hypertension often occurs but it need not be an essential in the diagnosis, nevertheless in the 2 cases referred to there was persistent hypertension, the blood pressure varying at first but ultimately becoming constant. It is emphasized that the blood pressure may be variable, but this does not necessarily bear any relationship to symptoms. For instance in one case during the attacks of sweating the blood pressure was normal, and *per contra* when the patient expressed herself as being perfectly well the blood pressure was often found to be high. One patient was found to have severe diabetes mellitus with polyuria of excessive degree, 16,800 cubic centimetres of urine being passed in 24 hours.

Treatment—An accurate diagnosis before operation in one of the cases resulted in successful surgical treatment and complete cure.

Deanesly, R., and Parkes, A. S. (1937) *Proc R Soc Med*, S B, 124, 279.

Ferrebee, J. W., Ragan, C., Atchley, D. W., and Loeb, R. F. (1939) *J Amer med Ass*, 113, 1725.

Hartman, F. A., Lewis, Lena A., and Toby, C. Gwendoline (1938) *Endocrinology*, 22, 207.

Ryan, E. J., and McCullagh, E. P. (1940) *Cleveland clin Quart*, 7, 19.

McCullagh, E. P., and Engel, W. J. (1942) *Ann Surg*, 116, 61.

Simpson, S. L. (1938)¹ *Lancet*, 2, 557.

— (1939)² *Proc R Soc Med*, 32, 685.

Thorn, G. W., Howard, R. P., and Emerson, K., Jun. (1939) *J clin Invest*, 18, 449.

Turnoff, D., and Rowntree, L. G. (1941) *J Amer med Ass*, 116, 2016.

Wilkinson, J. F. (1939) *Proc R Soc Med*, 32, 689.

AEROPHAGY

AETIOLOGY

The gas bubble present under the diaphragm and revealed by radiography is derived from the air swallowed with food and drink, the only condition in which it

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is absent is achalasia of the cardia, in which the contents of the oesophagus prevent the air from passing into the stomach. This air bubble is prevented from abnormally increasing by unconscious silent eructation, and by passage through the pylorus when in the horizontal position. If the normal expulsion is prevented, enormous quantities of gas collect, producing the condition of *aérogastrie bloquée*, this may be caused by spasm of the lower end of the oesophagus set up by an oesophageal ulcer or by dislocation of the cardia, generally due to excess of gas in the splenic flexure.

Hurst, A (1938) *Brit med J*, 1, 661

AGRANULOCYTOSIS

AETIOLOGY

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The main factors in the causation of agranulocytosis appear to be the synthetic drugs which have profound effects on susceptible persons, although according to Reznikoff^{1, 2} other factors, such as fatigue, worry and insomnia, also play a part in its onset.

Knowledge of the dangers of the use of amidopyrine together with restrictions have reduced considerably the number of cases ascribed to it. Experiments have shown that patients recovering from agranulocytosis are particularly sensitive to even small doses of amidopyrine (Plum, Israels and Wilkinson), and patients showing similar sensitivity without symptoms of agranulocytosis have also been described. The subject is very well discussed by Plum, who demonstrated that small doses of the drug given to sensitive subjects diminish the number of immature granulocytes in the marrow and of the granular cells in the circulating blood.

Cases of agranulocytosis are still reported after the use of gold and arsenical preparations, and less often after the barbituric acid derivatives. The main causes, however, appear to be the newer synthetic drugs used in the treatment of infections with streptococci, gonococci, meningococci, pneumococci and *B coli*. Quite a large number of cases of agranulocytosis, mainly fatal, have been reported after the use of drugs, such as prontosil, sulphanilamide, sulphapyridine (2-sulphanilyl-amidopyridine) and uleron (dimethyldisulphanilamide), and leucopenia and neutropenia have also been described (Whitby,^{1, 2} and many others). Colebrook drew attention to the danger attached to the use of these drugs and concluded that there is not much margin between the amount necessary to control a severe streptococcal infection (20 to 30 grammes of sulphanilamide) and that amount (30 to 60 grammes) which may initiate an attack of agranulocytosis in susceptible individuals. He emphasized the importance of frequent leucocyte counts, especially when the total dosage is 25 grammes or more, if the temperature is not showing a prompt response, or if there are any other toxic signs, such as headaches.

Owing to war-time conditions many people are working with toxic substances, for example solvents and trinitrotoluene in filling in chemical factories. If by chance such persons contract venereal disease and have to undergo arsenical treatment it is very dangerous to continue the treatment without most careful observation of the patient. In fact it is stressed that the practitioner or the venereologist in the areas in which such working conditions exist should find out whether it is possible that the patient may have been already infected by his or her proximity to such chemicals or the dust arising from them.

TREATMENT

Specific treatment

Control of the agranulocytosis

Pentnucleotide is still the most satisfactory form of treatment for the condition (Israels and Wilkinson, Wilkinson and Israels, Jackson and Tighe) although 1 gramme of adenine sulphate intramuscularly 3 times daily (Reznikoff^{1, 2}), yellow bone-marrow or extracts (Giffin and Watkins, Marberg and Wiles^{1, 2}), and transfusions of blood from leukaemic patients of the same group (Ravina, Bock) have all been reported to have given satisfactory therapeutic responses.

Prevention of relapses

Undoubtedly the most important prophylaxis is discontinuance of the drugs concerned, when this is not possible, the greatest care must be taken in their use—regular blood examinations (particularly total and differential leucocyte counts) being made, and administration immediately stopped when the slightest signs of intolerance or toxic reactions, however mild, are noted. Prolonged courses of sulphanilamide should be avoided at all costs.

Bock, H. E. (1937) *Fortschr. Ther.*, 13, 537

Colebrook, L. (1939) *Lancet*, 2, 158

Giffin, H. Z., and Watkins, C. H. (1938) *Minn. Med.*, 21, 62

Israels, M. C. G., and Wilkinson, J. F. (1937) *Quart. J. Med.*, 6, 35

Jackson, H., Jun., and Tighe, T. J. G. (1939) *New Engl. J. Med.*, 220,

AGRANULOCYTOSIS—ALCOHOLISM

- Marberg, C M, and Wiles, H O (1937)¹ *J Amer med Ass*, **109**, 1965
 — (1938)² *Arch intern Med*, **61**, 408
 Plum, P (1937) *Clinical and Experimental Investigations in Agranulocytosis with special reference to the Etiology* Copenhagen
 Ravina, A (1937) *Pr med*, **45**, 1760
 Reznikoff, P (1933)¹ *J clin Invest*, **12**, 45
 — (1938)² *Amer J med Sci*, **195**, 627
 Whitby, L E H (1937)¹ *Lancet*, **1**, 1517
 — (1938)² *ibid*, **2**, 1095
 Wilkinson, J F, and Israels, M C G (1934) *Lancet*, **2**, 353

ALCOHOLISM

THE TOXIC EFFECTS OF ALCOHOL

Chronic alcoholism

Aetiology

Biochemical considerations—Psychological factors have been investigated so thoroughly that there is very little more to be learned from them, on the other hand, in the biochemical field great advances have been made especially with regard to the carbohydrate metabolic action of vitamins. Since hypoglycaemia gives rise to a temporary psychosis and since in the treatment of schizophrenia the induction of hypoglycaemia has a good effect, sugar metabolism and general dietary factors have come into prominence. The biochemical theories are based on the fact that during the oxidation of sugar in the tissues stage by stage, energy is gradually produced, vitamin B is a very important link in this chain. If by the time the lactic acid stage of sugar metabolism has been reached vitamin B₁ is absent, subsequent oxidation is unsatisfactory and the substance, pyruvic acid, accumulates. It is now known that the typical peripheral neuritis of the chronic drinker is the result of deficiency of vitamin B₁ (aneurine). The lack of appetite and the gastric irritability of the person suffering from chronic alcoholism prevents the daily intake of the essential aneurine and thus it is clear why both central and peripheral neuritis is set up. As a proof of this the giving of aneurine, although it cannot be stored in the body, quickly reduces the severity of multiple neuritis. (See also Treatment below.)

Two factors at least are involved in the damage caused to nervous tissue by alcoholic excess, first its interference with the supply of essential vitamins and secondly its interference with the lipid material of the nerves. Both of these are fundamentally metabolic disturbances. The alcoholic, self-indulgent in all things and abnormal before ever he touches a drop, upsets his carbohydrate metabolism by over-indulgence in rich foods, later, in his efforts to side-step dull care and disagreeable reality, he seeks the oblivion procurable by over-indulgence in that quickly acting carbohydrate, alcohol. Such is the present biochemical, metabolic or dietetic side-light on alcoholism, its value from the preventive and therapeutic points of view is obvious.

Specific degenerative effects

Effect on the stomach—Drinks containing a small amount of alcohol, for instance beer, have practically no effect on the gastric mucous membrane, even the stronger alcoholic liquors such as neat whisky and the more potent wines do very little damage to the gastric mucosa when ample solid food is also taken. According to Hurst the results of taking alcohol on an empty stomach are first inhibition of secretion of the gastric juice, secondly excessive secretion of mucus and thirdly, if drinking is continued, the setting up of a subacute gastritis. Ultimately achlorhydria is likely to supervene and then chronic gastritis, the latter paving the way for primary carcinoma of the stomach.

The liver—Hurst also points out that before cirrhosis of the liver properly begins there is a condition of toxic degeneration which should rightly be termed hepatosis. Young men and women with the cocktail habit are peculiarly liable to this condition which can be completely cured if all alcohol is given up, and this despite the fact that the habit may have been indulged in for several months. Cirrhosis proper is set up only after many years of steady drinking. Eighty per cent of hepatic cirrhosis is caused by alcoholism and in this condition the majority of the alcoholic patients have lost their sense of taste and their appetite.

TREATMENT OF THE ALCOHOLIC

Detoxication

In acute alcoholic intoxication the stomach should be emptied first, and if the patient is strong and otherwise able to have it a subcutaneous injection of from $\frac{1}{10}$ to $\frac{1}{20}$ of a grain of apomorphine should be given, the danger here is that the patient might choke, as he is rather drowsy and naturally there is a considerable amount of vomiting after the apomorphine.

The alternative to this treatment is mechanical washing out of the stomach, as already mentioned in the *Encyclopaedia*, Vol 1, p 282. For the reactionary effects of

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an acute bout of drinking 5 cubic centimetres of a 10 per cent solution of leptazol should be given intravenously Practitioners should be alive to the possibility of methyl alcohol, generally referred to as 'Red Biddy', and drunk in considerable quantities by certain classes of people The danger here is acidosis and this must be neutralized by large injections of sodium bicarbonate solution

The long drawn out tapering process, at one time thought to be essential to success in the treatment of chronic addiction is now regarded as unnecessary, and abrupt withdrawal of alcohol—during a period extending over a few days only—is the most satisfactory method If paraldehyde is added to the whisky it makes the latter unpalatable and does not let the patient know how much whisky is being withdrawn, paraldehyde is also able to exercise its sedative action

Medicinal treatment and institutional control

Diet

In the treatment of alcoholism vegetables have always been recommended even before the substance, vitamin B, was known, this is analogous to the giving of lemon juice to sailors as a preventive of scurvy From what has been said above it is clear that the active principle of vegetables is aneurine All alcoholic patients may well be given the vitamin B complex with all its 8 components Wang and Harris have devised the thiochrome test for the estimation of aneurine in urine, by which (1) the resting level of excretion can be assessed and (2) the response to daily test doses of any preparation which may be given Thus if the urine of an adult male shows less than 90 μ g of aneurine the amount of vitamin B in his dietary should be regarded as inadequate and steps should be taken to remedy the defect

Hurst, A (1940) *Brit J Inebr*, **38**, 101

Wang, Y L., and Harris, L J (1943) *Brit med J*, **2**, 451

ALKAPTONURIA

SYMPTOMS

Ochronosis

Clinical picture

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About 50 per cent of cases of alkaptonuria are associated with ochronosis, and the condition is characterized by pigmentation of the cartilages, tendons, ligaments and the intima of large blood vessels In most cases the condition begins in infancy, is asymptomatic and lasts for some years, dysuria is noted occasionally In middle life the patient is debilitated, and the spine is rigid with a dorsal kyphosis There may be some swelling of the joints, and there is mottling and discoloration of the skin Radiologically the diagnosis may be made from calcification of the intervertebral disks tendon sheaths, bursal sacs and synovial membranes

Pomeranz, M M, Friedman, L J, and Tunick, I S (1941) *Radiology*, **37**, 295

ALLERGY

ALLERGIC DISEASES

Respiratory system

Hay fever

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Symptoms—Hypersensitivity to various pollens of the grasses gives rise to a type of paroxysmal rhinitis which in susceptible people sets up a congestion of the mucous membrane of the nose, throat and eyes According to Harley this normally occurs only during the pollinating season of the grasses which in England begins about the third week in May and lasts until the middle of July Symptoms are absent during the rest of the year but a reaction can be set up by the application of dried pollen or of pollen extract to the mucous membrane, these symptoms are typical of hay fever The asthmatical symptoms tend to become worse at the end of each hay fever season and with each successive year The term, hay fever, should be reserved for the pure grass pollen allergic reaction, the allergic rhinitis which is set up by tree, weed and flower pollens is properly designated 'ragweed fever'

Diagnosis—With modern methods of diagnosis more accurate categorization can be made, many of the former 'summer colds' being now recognized as hay fever Heredity is an important factor, as is well known, the allergic disposition is passed on from generation to generation but the manifestation may not be always that of hay fever The diagnosis should be confirmed by skin reactions Whether or not the skin reacts specifically to different grasses is still a debatable point, the grass pollens are immunologically allied very closely if indeed they are not identical For this reason Timothy pollen extract is ample as a test in the diagnosis of any kind of hay fever

Treatment—Desensitization by grass pollen extract given in graduated subcutaneous injections over a period of 2 or 3 months before the hay fever season starts is the most successful method of control Big doses should be given since these counteract any sensitivity of the patient's skin to pollen A typical course might begin with an initial dose of from 40 to 60 units, with very sensitive persons 10 or 20 units

might be more suitable. Twenty units' increase in dose every time a dose is given is continued until the dose reaches 200 units, after that at each successive dose a 15 per cent increase is made. Thus from 45 to 50 injections may be necessary in order that a top dose of from 20,000 to 100,000 units may be reached. The course should start at the beginning of March and end by the middle of May, 5 injections being given every week. Sometimes a reduced maintenance dose is given weekly during the hay fever season. In the unlikely event of the recurrence of a general reaction a subcutaneous dose of adrenaline will suffice. In many cases the patient may be taught to administer the injections to himself, 75 per cent of the patients who attend the Clinic at St Mary's Hospital, London, successfully inoculate themselves. It is not likely that a course of injections will be effective for more than one season, therefore second and further courses of treatment should be given each year. Recent work done shows that perennial treatment offers some hope of permanent cure, the maximum dose being given at fortnightly or monthly intervals for from 6 to 12 months after the maximum dose has been reached in the ordinary course of treatment.

If treatment is required when the hay fever season has begun it is satisfactory to give say from 10 to 40 units of pollen extract and 0.1 cubic centimetre of adrenaline (1 in 1000) at intervals of from 2 to 3 days. For the nostrils and eyes a mixture of adrenaline chloride (1 in 1000) 1½ fluid drachms, cocaine hydrochloride ½ grain, boric acid 20 grains, dissolved in 1 fluid ounce of distilled water is a palliative, the dose being 3 or 4 drops applied several times a day.

Efforts have been made recently to simplify desensitization by using pollen preparations which are more slowly absorbed from the point of inoculation, the dose may thus be more steeply graded. In the United States of America pollen protein hydrochloride and pollen in oil have been tested to a considerable extent and there has been some success. The methods which have not been of any avail are those of oral pollen therapy, histamine and histaminase treatment, oral potassium chloride therapy and zinc ionization.

Harley, D (1942) *Studies in Hay Fever and Asthma* London

AMENORRHOEA

TREATMENT

Ovarian hormones

Progesterone

Zondek describes a simplified treatment by progesterone with the omission or limitation of the use of oestrogen. For secondary amenorrhoea of more than 2 years' duration, a total dosage of 50 milligrams of progesterone is administered during a period of from 2 to 5 days, for secondary amenorrhoea of shorter duration the same dosage, or a total of 25 milligrams of progesterone, with from 2.5 to 5 milligrams of oestradiol benzoate, is given in 2 days. For primary or castration amenorrhoea, a total of 50 milligrams of progesterone with from 2.5 to 5 milligrams of oestradiol benzoate is given 5 days.

Zondek, B (1942) *J Amer med Ass*, 118, 705

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AMOEBIASIS

AMOEBIC DYSENTERY

Protozoology and pathology

Entamoeba histolytica

Life history—Winfield and Chin found by a study of faecal-borne diseases in China that up to 25.3 per cent of country family groups showed *E. histolytica* in their stools at a single examination, which according to others show only one-third of the total infections, this is therefore the highest incidence on record. Contrary to expectation, the proportion was lower in South China, where fresh human faeces are used for manuring, than in the north, where artificial manures are largely used, this may be due to the use of boiled rice in the south in place of hand-contaminated cold bread-stuffs in the north. There was a correlation between the incidence of amoebic and ascaris infections.

Incidence—Hegner, Beltran and Hewitt have carried out a survey of intestinal protozoa in Mexico and have found the high *E. histolytica* infection rate of 25 per cent. A familial incidence was shown by the fact that if one member was infected other members were more often infected than the general incidence would indicate.

Faust reports on post-mortem findings in amoebiasis in New Orleans. He agrees with other workers in America that all infections of the intestine with *E. histolytica*, including those in symptomless carriers, were associated with typical amoebic ulcers. Further light was obtained by the examination of the large intestine within 4 hours of death by accident in 202 cases, with the discovery of 13 cases of infection, 7 of which showed amoebic lesions, in 4 others amoebae were found throughout the large bowel and 2 showed minute infections with cysts. The lesions were mainly in the caecum-appendix region.

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Carriers—Sapero and Johnson have made extensive investigations regarding carriers of *E. histolytica* in men of the U S navy, mostly at Panama, after administration of a dose of cascara. The incidence of the parasite was 9.5 per cent, against 11 per cent among recruits, but no spread of amoebic dysentery was traced to the carriers even under close contact in naval vessels. There were only 4.6 per cent of dysentery cases for every 1,000 carriers. Taylor at Mukden, Manchuria, met with acute amoebic dysentery in 6 medical students, which he attributed to infection from a carrier cook.

Schoenleber found that 33 per cent of the native population in Venezuela were carriers of *E. histolytica*, among 1,500 immigrant Americans, whose infection rate in the United States is not more than 10 per cent, 25.57 per cent were proved to be carriers after a short residence in Venezuela. Active measures taken to control the spread of infection by food handlers without any other control reduced the percentage of infected Americans to only 1.92 during the next 3 years.

Clinical picture

Howell and Knoll report that the prevalent idea that amoebiasis is very rare in the young is not true of the United States of America, where the considerable rates of infection of 3.18 to 4.8 per cent were found in 2 institutions in which the incidence is highest. In children, intestinal symptoms and those simulating appendicitis were met with, these rapidly disappearing under emetine and carbarsone treatment.

Banerjee emphasizes the important practical point that less than half of the 133 cases of intestinal amoebiasis showed dysenteric symptoms. In many, dyspeptic signs were the most prominent feature. It was only after *E. histolytica* was found in the stools that most of them were correctly diagnosed and treated with prompt care. Sapero lays stress on the same point and records that 18 out of 47 anomalous cases of amoebic bowel infections showed symptoms of acute or chronic appendicitis. Mendelson records a case in which a very large amoebic granuloma of the caecum caused intestinal obstruction, revealed at an operation.

Ochsner and DeBakey in a comprehensive review of surgical amoebiasis point out that in the United States of America examination of the stools in every patient with a tentative diagnosis of appendicitis revealed that some 10 per cent of them had amoebic infections which were relieved by anti-amoebic therapy without the need for operation. Intestinal perforation of a most serious nature occurs in about 1.5 per cent of cases, nearly always in rapidly progressing fulminant cases. Secondary abscesses in the caecal region are more amenable to surgical interference, but such cases are liable to be mistaken for tuberculous or cancerous disease. Strictures of the large bowel in the caecal or sigmoid regions may rarely be met with.

Treatment

Drug resistance

Bonnin and Aretas^{1,2} exposed cultures of *E. histolytica* to increasing doses of emetine and obtained small amoebae with minute pseudopodia that became resistant to previously fatal concentrations of the drug. The amoebae retained some of this acquired resistance when they resumed their normal appearance on emetine-free media.

Treatment of polyneuritis

Alain and Ragiot found vitamin B₁ of use in the treatment of the polyneuritis that is liable to follow prolonged emetine treatment. They therefore advocate administration of vitamins when there are indications of intolerance to emetine.

Connell and French report good results in 8 out of 37 students showing symptoms and found microscopically to be infected, by the combined use of emetine and carbarsone. The amoebae disappeared from the stools within 3 days and no relapses occurred.

Mateer, Baltz, Marion and Hollands record 97 per cent cures among 104 cases of amoebiasis by the use of carbarsone orally, combined with yatren in enemas. Three patients who had relapsed were cured with vioform.

Craig reports on the use of drugs in the prophylaxis against intestinal amoebiasis. Carbarsone is too toxic in arsenical preparations to be taken for long. Diodoquin (5, 7-diiodo-8-hydroxyquinoline) is a compound in which chiniofon has been replaced by a second iodine atom forming a double iodine compound. It can be taken in large doses over a considerable period without ill effect. Chiniofon is a mixture of 7-iodo-8-hydroxyquinoline-5-sulphonic acid, 4 parts by weight, and sodium bicarbonate 1 part. It has amoebicidal properties and is given in doses of from 7 to 10, 0.21 gramme tablets daily, the smaller dose being used in chronic cases and cyst-passers, divided into 3 doses 1 after each meal for 20 days. If the patient remains in an endemic area for longer than 20 days the course may be repeated after a week's interval. Hummel also reports good results in 41 consecutive cases of amoebiasis using 10, 0.21 gramme tablets of diodoquin daily for 10 days. It is also of value in balantidiasis. Naidu found that use of the old Indian remedy for dysentery,

AMYLOID DISEASE—ANAEMIA

kurchi, or conessi bark (holarrhena B P C) was followed in the cases of 2 children by death, apparently from heart failure. The alkaloids of the drug were found in the viscera after death. As the drug is not very efficient, indiscriminate use is very dangerous.

AMOEBIC LIVER ABSCESS

Prognosis

Alport and Ghaliougui report that of 5 recoveries of very debilitated patients with liver abscess under the modern treatment of repeated aspirations and emetine injections, one patient required removal of 270 ounces of pus in 4 aspirations. Another recovered, in spite of pyocyanous infection, by treatment by aspiration and administration of prontosil and M & B 693.

Treatment

Berne records that many surgeons in the United States of America still treat these cases as purely surgical manifestations, with the result that at a California hospital the case mortality in 74 cases was 85 per cent (against 2 per cent in series of cases in India and in Korea treated by the reviewer's 1912 method of aspiration and emetine). On the other hand, in 19 cases treated by emetine alone all recovered on an average total dosage of $9\frac{1}{2}$ grains, and 18 patients treated by emetine and aspiration also all recovered. Cameron and Lawler advocate the replacement of the aspirated pus by air and taking 3 radiograms on the following day, namely from in front and from the side in the erect position and from in front in the recumbent one. This procedure allows the size of the cavity and the amount of residual pus to be determined, and later radiological examinations will furnish guidance to determine if further aspirations are required. Favourable results are reported in 12 cases.

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AMYLOID DISEASE

Imrie and Aitkenhead describe a case of amyloid disease in Still's disease. It is an example of the secondary type of amyloidosis in which there was not any evidence of any of the primary diseases usually associated with this condition. Necropsy showed amyloid changes in the liver, spleen and kidneys and to a small extent in the thyroid and the submaxillary glands.

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Imrie, A. H., and Aitkenhead, Anne C. (1939) *Lancet*, **2**, 421

ANAEMIA

MEGALOCYTIC ANAEMIA AND PREGNANCY

Megalocytic anaemia of pregnancy

Classification

The cases of microcytic or megalocytic type, found in pregnancy, can be classified into 3 main groups. The first consists of those who are already sufferers from pernicious anaemia and who are pregnant, in whom the demonstration of pernicious anaemia is emphasized because of the condition of pregnancy, the second contains those who are in the category of megalocytic or haemolytic anaemia, the third group

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comprises patients with tropical megalocytic anaemias. A point of great importance is that many patients with chronic anaemias which were in pre-war days well controlled and stabilized show degenerated conditions despite the fact that they are taking the usual amount of liver extract. It is obvious that such failing response to the remedy has its origin in scurvy and this is proved by the fact that when ascorbic acid is given the patients recover. Some other patients require extra supplies of desiccated hog's stomach, up to 30 grammes daily. Under war conditions it is advisable therefore to give in anaemic conditions a total of 30 grammes a day of desiccated hog's stomach by the mouth, divided into 3 doses. Otherwise if the anaemia is in an early stage, or as a part of the stomach therapy, liver extract may be given parenterally. It is advisable also to give vitamin C.

HYPOCHROMIC DEFICIENCY ANAEMIAS

Secondary group

Anaemia of pregnancy

The condition prevalent especially among pregnant women in war-time is the nutritional iron-deficiency hypochromic microcytic anaemia. Anaemia of this type appears generally during the last weeks of pregnancy or during the puerperium. When food is rationed and certain essential factors may be deficient the aetiology of the condition broadens considerably and factors such as vitamin C deficiency and lack of protein elements must be considered.

HAEMOLYTIC ANAEMIAS OF THE NEW-BORN

MacPherson, McCallum, and Haultain have shown that profound hypothermia is the characteristic abnormality in cases of spontaneous haemorrhage of the new-born, in cases of haemorrhagic disease, and icterus gravis neonatorum. They show that 'the introduction of vitamin K and more especially of vitamin K analogues into the clinical practice and the demonstration of the rapid elevation of the prothrombin index which follows the administration of these substances to the new-born' suggested another, and apparently specific, line of treatment for haemorrhagic disease, the successful use of which has already been reported in Europe and America.

Erythroblastosis neonatorum

Javert analyses, as a pathological obstetrical study, 47 personally observed cases of erythroblastosis neonatorum (erythroblastosis foetalis). This title covers the 3 closely allied, but clinically often different, conditions of hydrops foetalis, icterus gravis neonatorum, and congenital haemolytic anaemia. It is often difficult to classify a given case of erythroblastosis neonatorum under one of the above subdivisions, all of which have in common a varying degree of erythroblastosis, because the symptoms overlap and change. When the immature leucocytes are numerous the term erythro-leucoblastosis is sometimes used, as long ago as 1880 von Jaksch described his syndrome, and a haemorrhagic and an unclassified division have been suggested. Of his 47 cases Javert classified 22 as icteric and 16 as hydropic. Multiparity was regarded as an important factor in 92 per cent of the mothers. The first-born was seldom attacked but, when this did occur, other infants were especially liable to follow suit. The second, third or even the fifth may be the first to suffer. The mothers of erythroblastic infants with foetal hydrops are prone to pre-eclamptic toxæmia. The average weight of the 16 hydropic infants was 3,420 grammes ($7\frac{1}{2}$ lb), or 1,000 grammes ($2\frac{1}{2}$ lb) more than in a normal 36 weeks' gestation. Generally the hydropic infants show a higher degree of erythroblastosis and erythroblastæmia than do the cases of icterus gravis neonatorum. The hydrops infants are born a month before term, whereas the icteric infants come nearer to term. Asphyxia in the uterus, during birth or in neonatal life, is the most serious risk to the infants who show a high incidence of congenital abnormalities. The mortality for the hydrops cases was 100 per cent, and for the icteric cases was 54 per cent, dystocia during delivery may be due to ascites or to the large size of the infant. The immediate treatment of asphyxia is repeated transfusion from a compatible donor.

Rhesus factor

The Rhesus factor (Rh) is an antigen present in the erythrocytes of *Macacus rhesus*, and in about 85 per cent of human beings. Investigations show that if the Rh factor is present in the father and is transmitted to the foetus, it may, in a Rh negative mother, lead to the production of anti-Rh agglutinin, this may pass through the placenta into the foetal circulation and cause haemolysis. Such a mechanism may underlie the conditions of icterus gravis neonatorum, congenital haemolytic anaemia and hydrops foetalis, now classified together as erythroblastosis foetalis (Landsteiner and Wiener).

MICROCYTIC ANAEMIA

At a meeting in New York Rhoads discussed microcytic anaemia, particularly in relation to hookworm infection. In the Tropics the disability accompanying hookworm infestation appears to be due more to the severe anaemia produced than to the

parasites directly. In a well established infection this anaemia persists after the parasites are removed, but it is cured dramatically by the administration of iron. The anaemia is of the microcytic type, that is the erythrocytes are small and contain subnormal amounts of haemoglobin, and is analogous to iron-deficiency anaemias of temperate zones. Rhoads considers that the presence of microcytic anaemia is an almost certain indication of loss of blood, either chronic or intermittent haemorrhage, it very rarely results from a low intake of iron unless there is in addition loss of iron. In patients with hookworm infestation there is a chronic persistent loss of blood in the faeces and the hookworms themselves withdraw perceptible amounts. The presence of up to 1,000 hookworms may cause a loss of 10 to 20 cubic centimetres or more daily.

In observations on patients with hookworm infestation administration of a diet rich in protein and iron (300 grammes of meat and 1,000 cubic centimetres of milk daily) did not raise the level of haemoglobin appreciably, by supplementing this diet, without removing the parasites, with 6 grammes of iron and ammonium citrate daily the anaemia improved and symptoms disappeared.

Experiments designed to test the efficacy of liver in curing this microcytic anaemia showed that the Whipple fraction was effective, this is the alcohol-precipitated fraction and not the fraction which is effective in pernicious anaemia.

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ANAESTHESIA

CHOICE OF ANAESTHETIC

The nature of the operation

Vol. I, p. 475, para. 4 for the first sentence substitute the following: 'Preliminary narcosis and the use of scopolamine and morphine to a certain extent defeat the object of attaining this relaxation, but basal narcosis followed by spinal injection, or by local infiltration and splanchnic anaesthesia, gives admirable results in certain hands.'

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ETHER ANAESTHESIA

Methods of administration

Open method

Dangers—Vol. I, p. 482, lines 10 to 14. Delete the sentence 'In these cases ether.'

Intratracheal technique

Special indications—Vol. I, p. 484, line 5, the first word, 'with', should be altered to 'without'.

Technique—Vol. I, p. 485. At the end of Section 2 insert the following: 'The catheter should be lubricated with a 10 per cent pericaine ointment, or some similar grease, which makes coughing much less likely to occur.'

CHLOROFORM

Advantages and drawbacks

Danger of overdosage

Vol. I, p. 486. The whole of paragraphs 4 and 5 should be replaced by the following:

'The alarming fact in the use of chloroform is that death occurs with dramatic suddenness before the operation has been started, when there are no extenuating circumstances, such as haemorrhage or surgical shock, to share in the responsibility. This sudden death is due to ventricular fibrillation which may occur during an early stage of light anaesthesia, generally through the application of some stimulus.'

Technique of administration

In labour

Efforts have been made to put chloroform on a fool-proof basis of safety, for administration either by the nurse, or by the patient herself. This has been attempted by Mennell's simple, ingenious, and handy modification of Junker's apparatus, and by the introduction of capsules containing a limited number of minims of chloroform. When Mennell's apparatus is in use the patient herself squeezes the bulb which pumps the chloroform. However hard she does this only a weak vapour can be obtained for inhalation, and it is considered impossible for her to produce unconsciousness, but easy to achieve analgesia.

NITROUS OXIDE

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The use of nitrous oxide to control pain and discomfort during labour is now, owing largely to the efforts of Minnitt, being increasingly employed. The nitrous oxide and air apparatus designed by Minnitt is applied by the patient herself, by holding the face-piece to her face she delivers a proportion of nitrous oxide short of that needed for true anaesthesia.

CYCLOPROPANE

The use of cyclopropane as an inhalation anaesthetic has played an increasing part in recent practice.

Cyclopropane, which is chemically $\text{CH}_2\text{CH}_2\text{CH}_2$, requires comparatively complicated apparatus, for it must be given with a large proportion of oxygen and with the use of carbon dioxide absorption. When thus managed cyclopropane is a potent and valuable agent, for it is not irritating and, while capable of providing good relaxation, permits of very quiet respiratory movements, in fact in expert hands respiratory movement can be entirely abolished to enhance the surgeon's convenience without endangering the patient. By reason of this quiet form of breathing and the large amount of oxygen given with it, cyclopropane is especially well suited for the performance of chest operations on persons with serious lung damage, the only drawback being that, owing to the inflammability of the gas, diathermy cannot be employed on a patient during the inhalation of cyclopropane.

Cyclopropane is often employed to reinforce nitrous oxide. It cannot be regarded as so innocuous as the latter, for instances have been recorded of ventricular fibrillation associated with inhalation of cyclopropane and also of massive atelectasis following operations carried out under its influence. These have been explained as the result of the absence from the lungs of all inert gas when only cyclopropane and its accompanying large amounts of oxygen have been continuously inhaled for some time. The suggested prevention of pulmonary collapse lies in the introduction along with the cyclopropane and oxygen, of helium, an inert gas which is only slowly absorbed from the alveoli and thus saves them from collapse.

Experimentally cyclopropane has been proved to be almost without injurious effects on the liver or kidneys, and clinically this innocuousness has been equally demonstrated. On its first introduction cyclopropane was procurable only from America, now it is readily obtainable in Great Britain, where it is produced in quantities to meet the demand.

VINYL ETHER

Vinyl ether (divinyl ether), $(\text{CH}_2\text{CH})_2\text{O}$, has also a wide field of usefulness, differing from that of cyclopropane. It is especially well adapted for providing anaesthesia for short operations. It can in fact well replace ethyl chloride and act as a substitute for nitrous oxide when for any reason this is unsuitable.

Unlike cyclopropane, vinyl ether can be given by the simplest of means although its great volatility makes it unwise to administer it by open mask and drop-bottle. However it is given, vinyl ether must be freely diluted with air or oxygen. Great care therefore is needed when it is given from a closed apparatus, such as Clover's.

Action

Vinyl ether produces anaesthesia very rapidly, generally within a minute with the open method of administration. Within about 2½ minutes there is usually sufficient relaxation to allow of laparotomy. Since vinyl ether is rapidly eliminated, there is a quick return to consciousness when administration ceases. A small amount only is required for the induction of anaesthesia. In animal experiments it has been found that respiratory failure occurs before cardiac failure.

The anaesthetic effect of vinyl ether is said to be due to its solubility in fluids. It does not interfere with liver function, and evidence of liver damage has been found only in a few cases after prolonged administration. Wesley Bourne has shown experimentally that, in dogs, it does not enhance liver damage produced by chloroform, or alter the function of the liver. The risk of such damage is small since vinyl ether is chiefly employed for short anaesthetics.

The ratio of the anaesthetic to the lethal dose of vinyl ether is 1 : 2.4, whereas with ethyl ether and chloroform it is 1 : 1.5. Because of the rapid action of vinyl ether, however, special care to avoid overdosage should be taken, but, because of the rapid recovery rate, care must also be taken to maintain an even level of anaesthesia. Profuse salivation may occur, but this can generally be prevented by the pre-anaesthetic use of atropine. Post-operative nausea and vomiting seldom occur, and pulmonary complications are rare.

Advantages

Vinyl ether produces excellent muscular relaxation, comparable to that by chloroform, and perhaps better than that by ethyl ether. It has not the irritant effect of the

latter on the respiratory tract, and so may be employed in lung conditions in which ethyl ether is contra-indicated. Its rapid action, and the readiness with which a change-over can be made to ethyl ether, has led to its use by some anaesthetists in the induction of anaesthesia.

It does not cause cardiac depression as does chloroform, and the risk of post-operative liver damage and acidosis is negligible. The recovery period is more pleasant than that from ethyl ether or chloroform. Its use as an adjunct to nitrous oxide or ethylene does not increase the tendency of these gases to produce anoxaemia.

Disadvantages

Its rapid action and the low concentration necessary for the production of anaesthesia may lead to too high a concentration in the blood, unless care is taken in its administration. Its odour is objected to by some patients, but can be masked by the addition of eau-de-Cologne.

Uses

For short operations on children vinyl ether may be regarded as the best available inhalation anaesthetic. Nitrous oxide is often inconvenient for these patients, and ethyl chloride is not without risk. Vinyl ether has been extensively used with success for dental operations on the young. It is also very conveniently used in major surgery to reinforce continuous nitrous oxide and oxygen when relaxation is required. It is also employed in otorhinolaryngology, that is for tonsillectomy and myringotomy, in ophthalmology for fundus examinations in children, in orthopaedics for manipulation of bones and joints, in obstetrics for inducing anaesthesia during labour.

Administration

When it is desired to give vinyl ether for operations requiring something more than the single dose sufficient for dental and other quite short procedures, but not needing continuous gas and oxygen supplemented by vinyl ether, the apparatus designed by Kaye of Melbourne renders easy the continuous administration of vinyl ether and oxygen. The apparatus is not complicated or massive, but provides a flow-meter and carbon dioxide absorption. Good results have followed the use of an anaesthetic mixture consisting of 25 per cent vinyl ether and 75 per cent ethyl ether. The stage of induction is short, anaesthesia occurring in from 40 to 60 seconds, preceded by a brief period of excitement. Breathing is somewhat shallow and rapid during anaesthesia, but the respirations are smooth and equal in volume. A slight flushing of the face is usual, but there should be no cyanosis. Concerning the eye signs, the eyelids and recti muscles of the globe are slow to relax, the palpebral and conjunctival reflexes disappear, but the pupillary reactions are irregular, and the pupils repeatedly change in size. There is often sufficient muscular relaxation for operating while the lid and eyeball are still moving. The eyeballs oscillate even during deep anaesthesia. Recovery is rapid, compared with ethyl ether or chloroform, and is as rapid as after gas and oxygen. There is rarely excitement, and very rarely nausea or vomiting.

SPINAL ANAESTHESIA

Scope and limitations

Mention must be made of the application of spinal analgesia to thoracic surgery, for certain lobectomies and thoracoplasties it is regarded as the method of choice.

Technique

Stovaine and novocain

The 'feel' of the needle—Vol I, p 492, line 20. The new sentence should begin 'In the young, injection is easy.'

Etherington Wilson technique

In the Etherington Wilson^{1,2} technique, which is as warmly recommended by some as it is decried by others, and which was designed after much experiment with coloured solutions and glass tubes, a hypobaric solution of percaine is introduced into the cerebrospinal fluid at the third lumbar interspace, the patient being in the sitting posture which is maintained for a timed number of seconds according to the height of the desired anaesthesia. The patient is then placed on his back, and the table tilted to a measured amount of Trendelenburg inclination. Preliminary injection of scopolamine hypodermically is recommended by the author of the method.

LOCAL ANAESTHESIA

Regional anaesthesia

Patrick describes a technique for blocking the brachial plexus with which he obtained complete anaesthesia in 43 out of 44 cases. In this he does not depend on subjective symptoms in determining where the injection should be made but, employing a large volume of solution (60–70 cubic centimetres of a 2 per cent solution of novocain) he infiltrates widely over the first rib, creating a broad barrage zone which intersects the course of the brachial plexus.

Epidural injection

Dogliotti's innovation of epidural injection, whereby the injected anaesthetic solution does not enter the spinal canal but bathes the roots after they leave the cord, has found few followers in Great Britain. It has been a good deal practised in America without apparently arousing enthusiastic support. Injection through the sacral hiatus into the thecal canal is practised with success for operations on the perineal regions and groins.

RECTAL ANAESTHESIA AND BASAL NARCOSIS

Basal narcosis

Premedication

Recent years have seen an enormous increase in the employment of barbituric compounds in association with anaesthesia. They are used both in preliminary medication, and as basal narcotics, or as anaesthetics *per se*. For preliminary medication nembutal is probably the most widely used, 1 capsule being given the night before and 2 an hour before operation. This oral administration of the drug usually brings the patient to the operating table either unconscious or at least in a drowsy indifferent unalarmed state of mind. The effect, however, is not so certain as if the drug is given intravenously. Some anaesthetists prefer this, and give the nembutal as a basal narcotic half an hour or so before operation.

The two other popular barbiturates, evipan and pentothal, if used in association with other anaesthetics are given intravenously just before the main anaesthetic is to be administered. Their action is rapid and their effect does not last long. They are much used by themselves as anaesthetics for short operations. The pleasantness of induction of unconsciousness and the simple technique must not lead anaesthetists to replace by these agents nitrous oxide whenever this meets the case, for there is no comparison between nitrous oxide and the barbiturates as regards freedom from risk. Moreover, after all the barbiturates, there is the chance of prolonged restlessness and excitement such as is never seen after 'gas'.

Barbiturates are not always the best form of premedication. There is at the moment too great a tendency among anaesthetists to adopt some favourite form of premedication or basal narcotic, and to employ it as a routine without reflecting on the exact object of premedication in the particular case. Premedication and basal narcosis offer immense advantages, but these are only fully reaped if they are given according to a precise idea of the physiological action involved, and of the object in view. For example, one great advantage of suitable premedication is that it enables the safe anaesthetic, nitrous oxide, to be used efficiently on patients who otherwise would have to be submitted to the action of anaesthetics which are tissue poisons. This is brought about by using as the basal narcotic a drug or drugs which lower the basal metabolism. This lowers the oxygen need of the patient, and thus the anaesthetic nitrous oxide which must be given with limited amounts of oxygen is enabled to fill the bill perfectly well. In such a case a full dose of omnopon and scopolamine, or a smaller dose of these and an injection of avertin, is the proper premedication, and is superior to any barbiturate in bringing about the quiet breathing desired. Such a condition is wanted, for example, in upper abdominal operations when deep anaesthesia is necessary and when this without premedication leads to vigorous action of the diaphragm, and intercostal paralysis resulting in an abdominal heave which is exactly what the surgeon most dislikes. Barbiturates on the other hand are admirably adapted to eliminating in the patient that psychic element which may play so obnoxious or even disastrous a part in anaesthesia. Ventricular fibrillation is known to have a predisposing factor of adrenal hyperactivity as well as the precipitating factor of surgical or other stimulus. Emotional disturbance is a prime cause of adrenal hyperactivity, and thus it is that by obviating emotion the barbiturate or other suitable sedative lessens the risk of fibrillation. Moreover, fibrillation is not the only phenomenon that the anaesthetist fears in really nervous or apprehensive subjects. These people react unfavourably to their anaesthetic not only during the initial stages but throughout the operation, when they are disposed to muscular contraction and movement to an extent quite absent from the naturally placid individual. These awkward tendencies are also greatly controlled by due preliminary medication.

Another fact often overlooked when the preliminary drug is chosen is that atropine is a metabolic stimulant, and should therefore not be given before gas and oxygen. The chief aim of preliminary medication and basal narcosis besides those which have been mentioned is to enable the patient to be efficiently anaesthetized with the comparatively harmless gaseous anaesthetics, nitrous oxide and cyclopropane. Obviously care must be taken that this object is achieved without injurious effects due to the preliminary drugs themselves. Want of this care has led to condemnation of preliminary medication and to the attribution to it of pulmonary after-effects which arise not from its use but from its abuse.

Pentothal sodium

Pentothal sodium is closely related to nembutal (sodium ethyl methylbutylbarbiturate) and to sodium amytal (sodium isoamylethylbarbiturate)

Action

Pentothal sodium powerfully depresses the respiratory centre, affecting the amplitude rather than the rate of respiration. Overdosage from too rapid administration, or from excessive amounts readily produces cardiac, hepatic, and cerebral damage, from anoxia. Cyanosis is never a troublesome factor. Laryngospasm, trismus, sneezing, coughing, and hiccup occasionally occur, even during deep anaesthesia. Prevention and relief are readily obtainable by the injection of atropine. When severe overdosage is avoided and oxygenation is adequate, toxic effects on the circulatory system are negligible. There is generally a fall in blood pressure, although this is rarely marked. When properly administered pentothal sodium causes little change in the pulse rate.

The drug is destroyed in the liver, and, for this process, an adequate reserve of glycogen is necessary. There is no real evidence that harmful effects on the liver have occurred.

With regard to the kidneys, neither the normal nor the nephritic kidney is adversely affected, and renal disease is not a contra-indication to the use of the drug.

Advantages

The induction stage is rapid and pleasant, and there are rarely nausea and vomiting on recovery. The element of psychic shock is obviated, and patients take pentothal readily for subsequent anaesthetics. The use of narcotics for the relief of pain and restlessness for the first few hours after operation is minimized, and is often unnecessary. Post-anaesthetic nursing is reduced to a minimum.

Disadvantages

The use of pentothal for deep anaesthesia is, in inexperienced hands, not as safe as ether, because the anaesthetist has to depend on a type of respiration characteristic of the drug. The anaesthetist must therefore be familiar with this type of breathing, if it is to serve as a guide to the depth of anaesthesia. The action of pentothal varies greatly in different patients, and even in the same patient at different anaesthetics. Since premedication is necessary, pentothal is not well suited to emergency abdominal operations. Being administered intravenously, its use may be difficult or even impossible in patients with small veins.

Uses

Pentothal sodium may be employed as a total anaesthetic, for rapid and pleasant induction of anaesthesia preliminary to the use of ether or gas, as a basal narcotic, particularly in gas anaesthesia, as a supplement to local or spinal analgesia, especially when the latter is imperfect, in essential hypertension, for estimating the probable value of surgical treatment, as a therapeutic measure for combating the toxic effects of local anaesthetics, for use in convulsive states such as strychnine poisoning, tetanus, and eclampsia, as a sedative in maniacal states and narco-analyses (Marshall).

Pentothal sodium is generally given intravenously, though it may be administered orally or rectally, particularly in obstetrics. Given intravenously as a basal narcotic it greatly facilitates the administration of nitrous oxide and oxygen, allowing adequate anaesthesia without suboxygenation. Used thus it also allows of economy with the use of cyclopropane which is an expensive gas.

Pentothal sodium is indicated for minor and short operations, operations on the face, head, neck, and upper chest, in operations in which the use of the cautery, or diathermy, might lead to ignition of inflammable gases, in orthopaedic operations for the removal of adhesions, and reduction of fractures and dislocations, in minor urological procedures such as cystoscopy, ureteral catheterization, lithotripsy, passage of sounds, in ophthalmic surgery, in minor otorhinolaryngological procedures such as myringotomy and antral puncture, in short dental and oral procedures, in minor neurosurgical procedures, such as lumbar puncture, for nervous and mental patients who fear an anaesthetic mask, as a sedative in maniacal states, for patients suffering from acute diseases of the throat, bronchi, and lungs, such as coryza, bronchitis, early pneumonia, and early pulmonary tuberculosis, to combat convulsive attacks, as in strychnine poisoning, as a basal narcotic or adjuvant to other agents, in most major surgical operations other than those on the upper part of the abdomen, for bronchoscopy and oesophagoscopy to alleviate distress, and in cases in which there is need for reduction of more potent and toxic supplementary anaesthetics, for the production of anaesthesia during labour.

Contra-indications

The contra-indications to the use of pentothal sodium are chiefly referable to the depressant effect of large doses on the respiration, and to the probable state of the hepatic function. The absolute contra-indications, which are few, depend largely upon the availability or otherwise of facilities for resuscitation, particularly

the administration of oxygen. The drug should not be used in advanced pulmonary diseases, or in conditions causing mechanical obstruction in the respiratory apparatus. It should be used cautiously in operations on the larynx and pharynx, because the throat reflexes remain active in most patients, even under deep anaesthesia. Most authorities agree that pentothal is detoxified by the liver, and should not be used in advanced disease of that organ. Starvation from trismus or pyloric obstruction, leading to a low glycogen reserve, contra-indicates its use, as does also uncontrolled diabetes mellitus, which connotes a low glycogen reserve. Extreme renal impairment may be a contra-indication. The drug should not be used for operations on the upper part of the abdomen, since respiratory depression will hinder the introduction of supplementary agents. Severe cardiac decompensation, coronary disease, myocardial degeneration and low blood pressure are contra-indications, as are also severe toxæmia and pyrexia which may gravely impair cardiac and hepatic functions. Obese myxoedematous and extremely ill patients are not good risks. It should not be employed in severe anaemia, since in this condition the oxygen-carrying capacity of the blood is impaired. Long operations with the patient in the sitting position contra-indicate its use. Children under 10 years of age do not tolerate it well, because of their susceptibility to respiratory depression. If sulphanilamide has been given, there is an increased risk of sulphaemoglobinaemia.

Premedication

This is necessary because, in cases with associated pain, much larger doses are required to produce the desired effect if premedication is not given. In the attempt to keep the patient quiet an overdose may result.

Ideas with regard to premedication vary. Marshall holds that premedication is unnecessary for very brief and superficial procedures, that atropine is essential, and morphine advisable, in the more lengthy procedures, especially when pentothal is to be the only anaesthetic. The doses recommended are atropine, $\frac{1}{80}$ to $\frac{1}{60}$ grain, morphine, $\frac{1}{8}$ to $\frac{1}{4}$ grain. Atropine is essential, and morphine optional, when pentothal is to be used for basal narcosis. Morphine is best omitted in intra-abdominal work, since it favours the earlier onset of respiratory depression. Doses: atropine, $\frac{1}{80}$ to $\frac{1}{60}$ grain, morphine, $\frac{1}{8}$ to $\frac{1}{4}$ grain. If vomiting is likely, morphine should be replaced by diamorphine, $\frac{1}{12}$ to $\frac{1}{8}$ grain. Hyoscine should be avoided. The use of other barbiturates is undesirable, since they tend to increase restlessness, and possibly have cumulative effects. Some authorities, however, employ one of the more slowly acting barbiturates, such as sodium amytal or nembutal. Premedication should be given at least an hour before the anaesthetic.

Technique of administration

Administration of pentothal sodium is by fractional or intermittent injections. The amount necessary to produce anaesthesia varies greatly in different patients, and often in the same patient at different operations. In general, young, active, or nervous patients will require more than the old, placid, or cachectic. The same variation often applies to the maintenance dose. The drug has a cumulative effect, the longer the anaesthesia the less amount of the drug being necessary to maintain anaesthesia. The injection of pentothal sodium is made at the rate of about 1 cubic centimetre of the 5 per cent solution every 5 seconds, the patient being asked to count slowly. When he ceases counting, the amount of solution injected should be noted, and half as much again as has been injected given. After from $\frac{1}{2}$ to 1 minute relaxation is generally complete, and the operation may be begun. This amount will generally allow of an operation lasting a few minutes. If a longer anaesthesia is required, the needle should be kept in situ, and supplementary injections of 0.25 to 1 cubic centimetre given as required. These supplementary injections required will become progressively smaller and less frequent as the anaesthesia proceeds.

Course of anaesthesia

The chief characteristic of the anaesthesia is the type of respiration, which becomes progressively shallower with the depth of anaesthesia. Soon the jaw relaxes, and the tongue falls back, causing respiratory obstruction which may be easily overlooked owing to the speed with which this stage is reached. Throughout anaesthesia the chin must be supported firmly in order to maintain a clear airway. The absence of congestion in the nasal passages enables the mouth to be completely occluded in oral procedures. Lightness of anaesthesia is indicated by the increasing depth of respiration. Obstruction, however, will also increase respiratory efforts. Slight movements, phonation, and frowning are other signs of the lightness of anaesthesia. If anaesthesia is deep enough the corneal reflex is either sluggish or absent, the eyeballs are fixed, the eyelids are flaccid, and the pupils are contracted or semi-dilated and react to light. If the airway is clear, the colour remains good, in spite of the shallow breathing, but if there is cyanosis, this connotes either severe respiratory depression or respiratory obstruction. In such circumstances any obstruction should be removed, and coramine injected. Inhalation of saliva, blood, or vomited matter, or the attempt at tracheal intubation may lead to a persistent laryngospasm. Intra-tracheal insufflation of oxygen should be made.

ANGINA PECTORIS AND CORONARY THROMBOSIS

The time of recovery from pentothal sodium is roughly proportional to the amount of the drug administered. Prolonged unconsciousness is generally due to overdosage or delayed elimination. If post-anaesthetic depression appears to be deep, from 5 to 10 cubic centimetres of coramine should be given intravenously, repeated if necessary.

Kaye, G (1938) *Med J Aust*, 2, 856

Marshall, S V (1939) *Med J Aust*, 3, 382

Patrick, J (1940) *Brit J Surg*, 27, 734

Wilson, W E (1934)¹ *Brit J Anaesth*, 11, 43

— (1936)² *ibid*, 13, 108

ANGINA PECTORIS AND CORONARY THROMBOSIS

ANGINA PECTORIS

Treatment*Prevention of attacks*

For a considerable period Lesser has been treating patients with angina pectoris by giving them testosterone propionate. In the most recent series there were 21 men out of a total of 22 patients. All were relieved by the treatment, which was given in the form of injections, 25 milligrams being given at varying periods—from 2 to 5 days' interval. The average number of injections was 11 but some required as few as 5 and some as many as 25. There was no doubt about the efficacy of the treatment, attacks were reduced in number and their severity and duration were lessened. Most indeed were able to do more work after the treatment. Improvement was maintained without further treatment for from 2 to 12 months after the last injection was given. The patients were more comfortable, exercise tolerance was very much increased and when an attack did occur it was of a minor character. Relief from symptoms was followed shortly afterwards by disappearance of typical signs.

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CORONARY THROMBOSIS

Aetiology*Litigation and coronary thrombosis*

In litigation arising from insurance cases and especially so far as the Workmen's Compensation Act is concerned coronary thrombosis assumes much greater importance than it did formerly. Willius considers that the medico-legal side of coronary thrombosis should be reviewed very carefully. There is no doubt that coronary thrombosis is on the increase. Furthermore the litigation in the past has not given a very clear lead for those pronouncing judgment on present-day cases. The onset of senility is accompanied more or less by coronary arteriosclerosis and as this is the basis of coronary thrombosis it is fairly obvious that errors may have been made in ascribing coronary thrombosis to strenuous exercise and to heart strain. A very important point about the aetiology of coronary thrombosis is that it is those who are in sedentary jobs rather than those who are doing active physical work who are most susceptible to the disease. Attacks have been known to come on when a person was resting or in bed at night. The arbiter in any dispute is therefore faced with a most difficult task so far as coronary thrombosis is concerned, for the aetiological responsibility is not quite clear.

Clinical picture*Complications*

Perforation—Perforation of the interventricular septum rarely occurs at the site of an infarction.

Cardiac aneurysm—Cardiac aneurysm also occurs, especially from an anterior infarction, it can be recognized by radiological and clinical signs (Parkinson, Bedford and Thomson). There is expansile systolic pulsation apart from the apex beat, the heart is enlarged to the left and deformed, adhesions are present between the heart and the chest or diaphragm, and the wall of the sac may be calcified. The contained clot may be the origin of an embolus.

Changes in the electrocardiogram

In addition to the changes in the 3 leads described in Vol I, p 569, changes have now been recorded in lead IV (the chest lead), these changes may in fact precede those in the other leads and remain in the late stages when the other changes are no longer seen.

Master, Gubner, Dack and Jaffe draw attention to 2 forms of cardiac infarction, (1) the well recognized form due to obstruction of the coronary arteries which is the end-result of a progressive process in a sclerotic blood vessel and (2) coronary insufficiency without acute coronary obstruction, originally clearly defined by Marshall Hall in 1842, which occurs whenever there is disproportion between the oxygen requirement of the heart and the coronary blood flow, for example when the work of the heart is increased or the coronary circulation is impaired. The lesion differs from that in coronary obstruction in which the infarct is large and extends from the endocardium to the pericardium. Coronary insufficiency, on the other hand, usually consists in disseminated foci of myomalacia chiefly under the endocardium,

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particularly of the papillary muscles and the interventricular septum. In spite of the morbid changes differing in these 2 forms of myocardial infarction, the clinical signs and symptoms may be identical and confusion may arise. The authors therefore analysed the electrocardiographic changes in 48 cases of recent coronary insufficiency proved to be free from coronary occlusion at necropsy and by examination of the coronary arteries throughout their course by horizontal sections. Coronary sclerosis was common, as was enlargement of the heart. The electrocardiogram of acute coronary insufficiency is characterized by the presence of a depressed RS-T segment and flattening or inversion of the T wave in one or more leads, it thus differs from the elevated RS-T segment and the presence of a Q wave usually seen in acute coronary occlusion. These electrocardiographic changes are correlated with the character of the morbid changes, thus the presence of a depressed RS-T segment is attributed to the sub-endocardial position of the infarction in acute coronary insufficiency.

Treatment**Diet**

The value of a low calorie diet is becoming increasingly recognized. For the first week at least, fluids only should be given. The Karell diet consists of 200 cubic centimetres of milk 4 times daily at intervals of 4 hours, with, if necessary, 200 cubic centimetres of water.

Bedford, D. E. (1939) *Trans med Soc Lond*, **62**, 165

Lesser, M. A. (1943) *New Engl J Med*, **228**, 185

Master, A. M., Gubner, R., Dack, S., and Jaffe, H. L. (1941) *Arch intern Med*, **67**, 647

Parkinson, J., Bedford, D. E., and Thomson, W. A. R. (1938) *Quart J Med N S*, **7**, 455

Willius, F. A. (1942) *Proc Mayo Clin*, **17**, 521

ANGIOMA**TREATMENT****X-rays**

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A revision must now be made in the opinion expressed about X-rays. Short distance X-ray treatment, the so-called contact therapy, is undoubtedly effective in some cases. The greatest care must be taken not to set up a violent reaction and thus produce X-ray scarring. X-rays in small doses—30 to 35 r—in a baby, applied once a week, are also very useful in healing up spontaneous ulceration. If a big dose of radiations is given with ulceration present sepsis and scarring result.

ANKYLOSTOMIASIS OR HOOKWORM DISEASE**TREATMENT****Medical treatment**

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Peery reports on the toxic effects of large doses of carbon tetrachloride, so much used in the treatment of hookworm infections. The most prominent lesions were scattered small haemorrhages particularly about the abdominal organs, liver necrosis chiefly in the central lobular zone, and granular degeneration of the cells of the convoluted tubes of the kidneys. Such toxic sequelae emphasize the importance of using the equally effective, but less poisonous, tetrachlorethylene in the treatment of hookworm disease.

Azmy Pasha and Zanaty report on the value of small blood transfusions in the treatment of ankylostoma anaemia. To get the best results the hookworm must first be expelled, and iron administered. Hookworm anaemia resembles idiopathic anaemia, both being due to chronic haemorrhage (see also p. 16). McKenzie found that vitamin B₁₂ in the form of brewer's yeast and betaxan, rapidly cured the oedema of hookworm disease after iron and a generous diet had failed to do so. He therefore suggests that the oedema is due to loss of vitamins in the blood through the action of the hookworms.

Of 51 cases of hookworm anaemia reported by Heilig and Visweswar from Mysore the blood condition of 37 was very much benefited by the giving of iron without previously carrying out deworming treatment. Forty-two per cent had a gastric acidity below 20, the control group having an acidity of about one-half that of the affected group. The blood condition improved quite independently of the state of the gastric acidity.

Azmy, S., and Zanaty, A. F. (1939) *J trop Med (Hyg)*, **42**, 263

Heilig, R., and Visweswar (1942) *Indian med Gaz*, **77**, 385

McKenzie, A. (1939) *Lancet*, **1**, 1143

Peery, T. M. (1938) *Arch Path*, **26**, 923

ANOREXIA NERVOSA**AETIOLOGY AND CLINICAL PICTURE**

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In a case described by Reiss it has been clearly demonstrated that hypofunction of the anterior lobe of the pituitary gland can become completely altered to hyper-

function in a very short time, once the process has been put into operation. The case described was that of a woman aged 22 years who was extremely emaciated and who after 18 months was obese. Similar states have been observed as occurring for instance after scarlet fever, and cases have been known in which adipose boys and girls have become thin after puberty, but this is the first time that a state of emaciation being transformed to that of adiposity has been reported. Incidentally the author suggests that the term, anorexia nervosa, should be dropped in favour of 'cerebral' pituitary cachexia.

Reiss, M (1943) *J ment Sci*, 89, 270

ANTENATAL CARE

THE OBSTETRICAL EXAMINATION

X-ray examination of the pelvis

Greater use is now made of radiological examination of the pelvis if there is the least doubt regarding the adequacy of the cavity. A lateral view showing the length of the true conjugate and the shape and curvature of the sacrum is the most useful, but an antero-posterior view is also of value as it shows the shape of the pelvic inlet and the pubic arch. The accurate information obtained by X-rays is especially desirable if external prophylactic version of breech cases has failed and delivery of the breech by the natural passages is contemplated.

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HYGIENE OF PREGNANCY

Diet

Of 5,022 cases investigated by a Committee of the People's League of Health, London, the detailed records of the weekly meals taken by 1,000 women were studied. Protein intake was found to be satisfactory but as a result of insufficient consumption of milk and cheese there was a shortage of calcium in 70 per cent of these women. In all but 2 per cent there was iron deficiency. So far as vitamin deficiency is concerned vitamins A, B and C were all lacking in the diets of half the number of women but the deficiency of vitamin A was most noticeable. The following daily supplement was then decided upon: saccharated ferrous iron 18 grains, calcium lactate 30 grains, traces of iodine, manganese and copper, a preparation of whole vitamin B complex 15 grains, ascorbic acid 100 milligrams, halibut-liver oil 6 minims. Two equal groups of women were formed, one receiving the above supplement, the other continuing to have ordinary diet and acting as a control. Of the primigravidae who received supplemented diet 27.1 per cent had toxæmia of pregnancy whereas those without supplement showed an incidence of 31.7 per cent, the difference was most distinct in women between 25 and 30 years of age. With regard to the multigravidae there was in both groups an incidence of toxæmia of 21.8 per cent and puerperal sepsis was unaffected.

Report (Interim) of People's League of Health (1942) *Lancet*, 2, 10

ANUS DISEASES

Definition

FISTULA IN ANO

The classification of fistula suggested by Milligan and Morgan, now widely recognized as a practical simplification, is as follows: (1) Subcutaneous and sub-mucous fistulae, (2) fistulae with main tracks entering the anal canal *below* the ano-rectal ring (anal fistulae) (a) low-level anal fistula and (b) high-level anal fistula, (3) fistulae with tracks extending *above* the ano-rectal ring (ano-rectal fistulae) (a) with internal openings into rectum, (b) without internal openings and (c) with main-track openings into the anal canal below the ano-rectal ring.

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Aetiology

PRURITUS ANI

A fungous infection may be responsible for pruritus ani. The mycotic infections may be caused by the epidermophyton, or yeasts of the type known as *Monilia albicans*. Clinically a mycotic cause may be suspected when a localized dermatitis is found round the anus with a well defined circumscribed edge.

Castellani described a state of pruritus associated with fungi, usually trichophyton-like fungi and yeast-like fungi, common throughout the Tropics and Subtropics and occurring also in temperate zones. The fungi might be secondary invaders. Coliform bacilli, *Bacillus mucosus*, *Bacillus proteus*, and various cocci have also been found. The bacteria probably cause a secondary eczematous dermatitis but it is doubtful whether they cause the pruritus. The monilial form is commoner in females than in males and is probably due to vaginal discharge containing monilia causing infection of the peri-anal and anal regions.

Treatment

Treatment is usually by local applications of Castellani's carbol-fuchsine paint, or by 1 or 2 per cent gentian violet in 20 per cent alcohol.

CUMULATIVE SUPPLEMENT 1945
CARCINOMA OF THE ANUS

Squamous-celled carcinoma

Pathology

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Of all cases of cancer of the rectum, anal canal, and anus admitted to St Mark's Hospital for Diseases of the Rectum, London, from 1922 to 1940, Gabriel found that the incidence of squamous-celled carcinoma of the anus and anal canal was 3.35 per cent. His review of these 55 cases shows that the sex incidence is practically equal, that is 27 males and 28 females, and the average age in male and female 61.7 years. The cases were divided into 3 grades of malignancy—low, medium and high. The low-grade cases showed well marked cell differentiation with much keratinization and numerous well defined cell nests. This type of squamous cancer is twice as frequent in men as in women and generally originates at the anal margin. The medium-grade cases are more cellular with little differentiation and few cell nests. They are equally distributed between men and women and may arise at the anus or in the anal canal. The high-grade cases are extremely cellular and undifferentiated, but keratinization is usually completely absent. They are much more common in females than in males and are almost entirely limited to the anal canal. One-third of the anal margin growths and one-half of the anal canal growths were in the anterior quadrant.

Differential diagnosis

Differential diagnosis must be made from simple papilloma, simple ulcer, chronic inflammation, tuberculous ulcer, tuberculide, primary chancre, amoebic ulcer, basal-celled carcinoma, columnar-celled carcinoma.

Treatment

Before undertaking treatment it is essential to grade the malignancy and reserve a piece for purposes of biopsy. Interstitial radium needling gives the best results in the early low-grade cases, but local excision with diathermy in early low-grade cases might give equally good results. In the medium grade, treatment is chiefly by colostomy or radium, or by a combination of both, but the results are disappointing and, including the high-grade cases, only 3 patients out of 33 showed 5-year survival, and in these excision of the rectum had been carried out. Low-grade cases treated in the early stage did not show any metastases in the inguinal glands. In all other cases of the series the inguinal glands were the seat of metastatic growth, and block dissection of these glands was performed in suitable cases 2 or 3 weeks after the treatment of the primary growth had been carried out.

Castellani, A. (1938) *J. trop. Med. (Hyg.)*, 41, 377

Gabriel, W. B. (1941) *Proc. R. Soc. Med.*, 34, 139

Milligan, E. T. C., and Morgan, C. N. (1934) *Lancet*, 2, 1150, 1213

APHTHOUS FEVER

TREATMENT

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The chief thing known about the treatment is that it is far from satisfactory, according to some American authorities the use of gentian violet is only to stain the child's face and most of his environment. They claim that more rapid immediate relief is obtained by swabbing the affected part of the mouth, one section at a time, with a 5-7 per cent solution of chromic acid in water, after a preliminary mouth wash with hydrogen peroxide. The chromic acid is applied twice daily for from 1 to 3 days and then once daily. But the duration of the disease is shortened only by 2 days (Smith and Johnson).

Smith, C. H., and Johnson, H. B. (1940) *J. Pediat.*, 17, 1

APPENDICITIS

ACUTE APPENDICITIS

Clinical picture

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Although the classical signs of appendicitis must dominate the condition generally of appendicitis it should always be borne in mind that variations of one or other of these signs is to be expected, much depending upon the individuality of the patient, the diagnosis of acute appendicitis must never be lightly discarded, and at all times the most exhaustive examination should be made. In the search for the acutely tender spot in the abdomen the various possible sites of the appendix should not be forgotten and the point of maximum tenderness may be elusive. The leucocyte count, the cytological reaction and bacteriology all have a certain important value, the last two might well become increasingly important in view of the possibility of sulphonamide treatment in the future.

Treatment

From 1940 onwards operation has been advised by most authorities, quite irrespective of the stage at which the disease might be. This is allowable when the appendix is unperforated, but if there should be delay and the patient is critically ill, sometimes pre-operative treatment by modern methods may render the subsequent operation much less dangerous. For this reason a few hours of resuscitation may

APHTHOUS FEVER—ARTERIAL DISEASE AND DEGENERATION

be of the greatest advantage The Miller-Abbott tube is very successful in relief for the nausea and vomiting associated with appendicitis Oxygen given by the B L B mask limits anaerobic development The giving of glucose and saline by the intravenous drip method replaces lost chlorides and restores the fluid balance Increased warmth provided by hot-water bottles and blankets or other sources of heat counteracts pain and shock

ARRHYTHMIA

AURICULAR FLUTTER AND AURICULAR FIBRILLATION

Auricular fibrillation**Treatment**

Ouabain—The cardiac tonic, ouabain (g-strophanthin), has been used by a certain number of physicians in cases of cardiac arrhythmia Geffer and Leaman in a series of 37 cases had 24 of auricular fibrillation The patients concerned as well as the others were treated by intravenous injection of 0.5 milligram of the drug and an hour later a large oral dose of digitalis leaf (4–8 cat units) was given Twenty-four hours later a daily course of digitalis (1 cat unit) was begun The ventricular rate was slowed down considerably in most of the patients and Geffer and Leaman consider ouabain to be a valuable aid to full digitalization, it was most successful in cases of congestive heart failure associated with rheumatic heart disease The toxic effects were rare

Geffer, W I, and Leaman, W G, Jun (1943) *Amer J med Sci*, **205**, 190

ARTERIAL DISEASE AND DEGENERATION

THROMBO-ANGIITIS OBLITERANS (BUERGER'S DISEASE)

Aetiology

The aetiology of Buerger's disease is still indefinite although streptococci have been discovered in some cases Allen asks 4 important questions and still awaits the answers (1) why are 99 per cent of the patients males? (2) why is the age of onset between 25 and 45 years whereas in arteriosclerosis it is between 55 and 85 years? (3) why are the Jews affected more than others? (4) why are the extremities, especially the lower limbs, affected more often than other parts of the body? Reports from China show that the Chinese and the Russians may also be affected It is not established that tobacco smoking is the primary cause of the disease

Treatment

The treatment of Buerger's disease by amputation is not to be encouraged because this surgical measure does not cure the disease Allen sums up the situation in general terms by saying that there should be a well planned programme of treatment in which physician, orthopaedic surgeon and neurosurgeon participate

CHRONIC ARTERITIS**Clinical picture***Thrombo-arteriosclerosis obliterans*

Hines and Barker report 280 consecutive cases of thrombo-arteriosclerosis obliterans seen at the Mayo Clinic from 1929 to 1933 This form of arteriosclerosis has been spoken of as 'arteriosclerosis with occlusion' and 'occlusive arteriosclerosis' It should be separated from thrombo-angitis obliterans (Buerger's disease) on the one hand and from ordinary arteriosclerosis on the other hand As compared with Buerger's disease there is not any significant racial (Hebrew) incidence The names 'senile gangrene' and 'diabetic gangrene' should, it is urged, be discarded, and thrombo-arteriosclerosis obliterans, shortened by omission of thrombo-, is regarded as a good descriptive title for this form of chronic arterial disease, which is stated to be rare The 3 essential morbid changes are atheromatous plaques in the sub-intimal tissue, degeneration in the medial coat and thrombosis There were not any important differences in the lesions of arteriosclerosis obliterans among patients with diabetes mellitus and those free from that metabolic disease Among the 280 cases analysed 240 were males and 40 females, 70 per cent were between 50 and 70 years of age, the youngest being 35 and the oldest 96 years Amputation was required in 70, or 25 per cent, of the patients, in 32 of whom the morbid changes were specially investigated

Treatment*Arteriosclerotic endarteritis*

Certain patients with considerable vasospasm can be benefited by blocking of the lumbar sympathetic system with procaine or by having sympathectomy done (Ives) In a small group of patients so treated the average age was 60 years The posterior tibial artery and the dorsalis pedis artery were pulseless although there was not any gangrene of the feet

Allen, E V (1942) *Bull N Y Acad Med*, **18**, 165

Hines, E A, Jun, and Barker, N W (1940) *Amer J med Sci*, **200**, 717

Ives, H R (1943) *Proc R Soc Med*, **36**, 339

ARTHRITIS: I—ACUTE ARTHRITIS
GONOCOCCAL ARTHRITIS

Treatment

- 95 According to Kersley the knees and ankles are the joints most often involved. Statistics of Army patients show that the average stay in hospital is 3.8 months. Treatment is varied and includes administration of sulphanilamide, fever therapy, ionization and other forms of physiotherapy. The most effective treatment appears to be that of hyperthermy especially when chemotherapy is also instituted.

Kersley, G. D. (1942) *Proc. R. Soc. Med.*, 35, 653

ARTHRITIS · II—RHEUMATOID ARTHRITIS
DIFFERENTIAL DIAGNOSIS

- 98 Stott and Copeman describe a series of cases seen in the British Expeditionary Force, some having been diagnosed as early rheumatoid arthritis. As the result of blood cultures, however, some of them were shown to be due to chronic meningococcal septicaemia. This syndrome is considerably commoner than has been previously believed, and should therefore be borne in mind as a differential diagnosis in the early stages of symptoms suggesting rheumatoid arthritis.

TREATMENT

Medicinal

Injection of gold salts

Chrysotherapy in the treatment of rheumatoid arthritis has been in vogue for many years and the consensus of opinion is that by its use better results are obtained than by any other form of treatment. Nevertheless in certain cases there has been a surprising degree of toxic reaction. Gold preparations of various kinds have been employed—organic, inorganic, soluble in water, insoluble in water, prepared in solution or given as colloids. The gold salts in use vary considerably in gold content and as a rule the salt which contains most gold is most efficacious. What happens when gold comes in contact with human protoplasm is not clearly known. Freyberg has investigated changes in the metabolism as the result of chrysotherapy, the gold content of the blood being determined as well as the amount of gold excreted during and after treatment. Gold may be discovered in the plasma and urine many months after the last injection of sodium aurothiomalate. Myocrisin which contains 50 per cent of gold is apparently the best drug to use. The dose should be increased gradually from 10 to 100 milligrams weekly until 1 gramme has been given. Toxic reactions are always a possibility and indeed it is agreed that satisfactory results cannot be obtained unless there is a certain amount of toxicity. It may also be mentioned that calcium aurothiomalate, a gold salt recently introduced for the treatment of rheumatoid arthritis, has been tested.

Orthopaedic measures

A very successful method of 'serial plasters', which is a compromise between rest and movement, has been introduced. The aim is to check the tendency to contracture, present in the joints of so many active cases, and at the same time to allow the inflammatory swelling around these joints to subside and disperse. The affected joints are put into a light plaster of Paris cast, in the best position obtainable. In some cases a brief anaesthetic, such as evipan, may be used with this object, but the joint should not be forced much beyond what it can achieve when the patient is conscious. After an interval, which should not exceed a week, this cast must be bivalved and the joint gently put through full movement. In nearly every case the short period of immobility will have reduced the swelling and, muscle spasm having also been relieved, the limb will be straighter and capable of freer movement than previously. This process may be repeated several times until the affected limb appears to be straight. When this has been done, the lower half of the last cast should be kept and used as a splint which the patient should wear at night for a month or two and he should also wear it during periods of the day if any tendency to contracture again occurs. That no unsplit cast be left on a limb for more than a week is an efficient safeguard against the occurrence of any ankylosis.

Freyberg, R. H. (1942) *Proc. Mayo Clin.*, 17, 534

Stott, A. W., and Copeman, W. S. C. (1940) *Lancet*, 1, 1116

ARTHRITIS · III—MENOPAUSAL ARTHRITIS
AETIOLOGY AND TREATMENT

- 99 In discussing the existence of menopausal arthritis as a clinical entity, Hall divided patients with joint disturbances during the menopausal period into 2 groups. (1) In some there is evidence of thyroid deficiency—the association of these conditions also occurred in men and in younger patients. (2) In others without evidence of thyroid deficiency, deficiency of ovarian secretion was regarded as an important causal factor. In 71 women with arthralgia or arthritic symptoms after removal or

ARTHRITIS

destruction of the ovaries, many of whom were treated with oestrogenic hormone, striking benefit followed, 53 of the patients were diagnosed as having arthralgia and 18 as having true arthritis, atrophic (rheumatoid), hypertrophic (osteoarthritic) and mixed types. To 40 of the 53 arthralgic patients oestrogenic hormones in sufficient dosage to control the menopausal symptoms were given, in 30 of these the arthralgic symptoms were entirely or practically relieved, and in 5 others they were much improved. Of the 18 arthritic patients, in 50 per cent the menopausal symptoms and the arthralgia were relieved, and in some cases the arthritis improved. For the arthralgic patients progynon B, the benzoic acid ester of oestradiol dissolved in sesame oil, was given intramuscularly. In some cases progynon D H tablets were given orally, but the intramuscular route was preferable. Failure of the earlier attempts at oestrogenic therapy was ascribed to inadequate dosage, it was found that larger amounts were usually required to control the arthralgia than to relieve the other menopausal symptoms. The usual dosage was 10,000 international units twice a week for from 4 to 6 weeks. Symptoms did not generally improve until the third week of treatment. In some cases 5 times this amount seemed a more adequate dose.

Murray confirms Hall's use of oestrogenic hormones. He combines spa treatment with intramuscular injections of oestradiol benzoate in amounts varying from 10,000 units twice weekly in early cases to 50,000 units twice weekly in advanced cases. In Murray's series most of the patients improved, some to a remarkable extent even in advanced stages of the disease. He suggests that stilboestrol may be used instead of oestradiol benzoate.

Hall, F. C. (1938) *New Engl. J. Med.*, **219**, 1015

Murray, J. A. (1941) *Brit. med. J.*, **1**, 590

ARTHRITIS IV—OSTEOARTHRITIS

AETIOLOGY

Incidence, distribution, and predisposing causes

Degenerative arthritis

Bauer and Bennett have shown that degeneration of the articular cartilage normally begins much earlier in life than was hitherto supposed, namely, from the third decade onwards. Many factors might expedite this aging process in the articular cartilage. Inheritance of a particular type of cartilage probably plays a part, but Bauer and Bennett lay even greater stress upon the traumatic factor. An isolated injury might start the train of changes or, on the other hand, a series of injuries or contusions, such as might be associated with certain occupations, appeared to be an important cause of early degenerative changes.

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TREATMENT

Surgery

Osteoarthritis of the hip-joint

Vitallium cup arthroplasty—Smith-Petersen describes a method of preventing restiffening of the hip-joint after arthroplasty by covering the reshaped femoral head with a mould composed either of glass (pyrex), 'bakelite' or vitallium, the last is a metal alloy consisting of chromium, cobalt and molybdenum. This type of treatment has been carried out in many places and successful results have been obtained especially when physiotherapy is employed in both pre-operative and post-operative stages. As a rule there should be about 3 weeks' pre-operative treatment.

Other surgical measures—In a series of 77 cases of osteoarthritis of the hip-joint Henderson and Pollock found that men predominated in the proportions of 55 to 22. The cases fell into 3 groups. In group (1) were cases in the earlier stages of the disease in which osteophytic developments were absent or slight. For these, manipulations alone or combined with bone drilling resulted in an appreciable improvement in a number of the patients. In group (2) hypertrophic changes were present in the articular margins of the acetabulum and femoral head and movement was very much restricted in all directions. In 3 cases cheilotomy and acetabulo-plasty and in a few cases reconstructive measures of the Whitman or Colonna type were performed. In group (3) were cases with pain as the chief complaint for which relief had not been obtained by physical therapy and rest. There was usually considerable distortion of the femoral head and acetabulum, the patients were treated by arthrodesis, which has given best results.

In cases associated with severe pain capsulectomy gives gratifying results. In advanced cases capsulectomy combined with acetabulo-plasty or with cheilotomy of the femoral head and acetabulum may be the most satisfactory form of treatment. In all cases the treatment comprises careful manipulations and early post-operative movements.

Bauer, W., and Bennett, G. A. (1936) *J. Bone Jt Surg.*, **18**, 1

Henderson, M. S., and Pollock, G. A. (1940) *J. Bone Jt Surg.*, **22**, 923

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ARTHROPODS AND DISEASE

ARTHROPODS AS TRANSMITTERS OF DISEASE

Biological transmitters

Flies

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Filariasis —The following additional species have now been proved to be efficient transmitters of *Wuchereria* (*Filaria*) *bancrofti* to man, in Batavia *Anopheles sundaicus* (Iudlowi), *A. subpictus*, *A. annulatus*, *A. vagus*, *A. tessellatus* (Soewadji Prawirohardjo)

The following mosquitoes are now known to be efficient transmitters of *Wuchereria* (*Filaria*) *malayi* to man From the Oriental Region (India) *Mansonia* (*Mansonioides*) *annulifera*, *M* (*M*) *uniformis*, *M* (*M*) *indiana*, *Armigeres obturbans*, and *Anopheles hyrcanus* var *nigerrimus* (Iyengar), (Malay) *M* (*M*) *longipalpis* and *M* (*M*) *uniformis* (Hodgkin) Far East (Tonkin) *Mansonia* (*M*) *indiana* (Galliard) and *M* (*M*) *uniformis* (Feng)

Leishmaniasis —Berberian records the successful mechanical transmission of *Leishmania tropica* by the bite of the stable fly, *Stomoxys calcitrans*, which had previously fed on a lesion

Malaria —As *Culex bitaeniorhynchus* breeds in pure water it has been suggested by Brug that it may be a suitable transmitter of malaria Williamson and Zain have carried out some experiments to test this Thirty bred females were fed on human blood containing large numbers of benign or malignant tertian malaria either separately or mixed, or on human blood containing quartan parasites mixed with less intense infections of malignant tertian Six mosquitoes showed sporozoites in the salivary glands and 2 others sporozoites in the salivary glands and elsewhere Of 23 females fed on the blood of malignant tertian cases, 6 showed sporozoites in the salivary glands

Yellow fever —Bennett, Baker, and Sellards have transmitted the virus of yellow fever by the bites of the mosquito *Aedes triseriatus* Patiño Camargo, by experiments, has proved that *Culex fatigans* is capable of transmitting the virus of yellow fever, also that *Aedes scapularis*, *A. taeniorhynchus*, *A. fluviatilis*, as well as *A. aegypti*, have been known to transmit the disease in Colombia

Roubaud, in discussing the transmission of yellow fever, particularly with regard to the possibility of the virus being introduced into Europe, shows that it may be experimentally transmitted by *Aedes geniculatus*, a mosquito found in forest regions of cold and temperate parts of the Continent

Shannon, Whitman, and Franka, when studying an outbreak of rural and jungle yellow fever, proved by feeding experiments that the mosquitoes *Aedes leucocelaenus* and *Haemagogus capricorni* transmitted the virus

Olsuf'ev pointed out that recent investigations into the epidemiology of tularaemia in the U S S R have shown that ticks of the genus *Ixodes* are among the chief vectors, when once infected with *Bacterium tularensis* they harbour it throughout life Other experimental vectors are *Cimex lectularius*, lice of the genus *Hoplopleura*, and tabanids *Stomoxys calcitrans* was able to transmit the bacterium for from 34 to 48 hours after the infecting feed In other experiments mosquitoes of the genus *Aedes*, *Anopheles* and *Mansonia* harboured the infection for periods of over a month and readily transmitted it by biting sheep and rodents Rodents also contracted the disease when infected mosquitoes were crushed on the scarified skin

Relapsing fever —According to Wheeler Californian relapsing fever is transmitted by the bite of *Ornithodoros hermsi*

Encephalitis —Encephalitis in man in Minnesota and Massachusetts has been shown by Riley to be due to the virus of equine encephalo-mylitis, and mosquitoes of the genus *Aedes* are the probable transmitters Riley has obtained experimental transmission with the following mosquitoes *Aedes* (*Stegomyia*) *fasciata* (*aegypti*), *Aedes albopictus*, *A. cantator*, *A. sollicitans*, *A. taeniorhynchus*, *A. dorsalis*, *A. nigromaculis*, and *A. vexans*

Tick paralysis —A recent review of the subject of tick paralysis emphasizes that the most outstanding features are an ascending paralysis of the Landry type One of the main points so far as treatment is concerned is to remove the tick before bulbar paralysis may arise Irritability is a prominent sign of the condition which is in existence before flaccid paralysis occurs, such irritability lasts for from 12 to 24 hours The speed of the spread of paralysis is very great, in a few hours there may be lingual and facial paralysis, with difficulty in swallowing and many other symptoms All reflexes are absent Abbott says that in every case of facial paralysis tick paralysis should be thought of, therefore a close examination should be made for the insects, which generally seek folds of the skin such as the groin, perineum, axilla, mammary folds, scalp and ears, the best method of removal is one in which gentle traction is used, and for the 'head parts' kerosene, gasolene, oil, chloroform and heat have been experimented with Sometimes even the affected portion of skin has been excised

ARTHROPODS AND DISEASE—ASPHYXIA IN CHILDREN

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 Berberian, D A (1938) *Proc Soc exp Biol, N Y*, 38, 254
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 Iyengar, M O T (1938) *Indian med Res Mem*, No 30
 Olsuf'ev, G N (1939) *Summaries of Reports of the All-Union Conference of Workers in Microbiology and Epidemiology and Infectious Diseases*, Moscow
 Patiño Camargo, L (1937) *Rev Fac Med Bogota*, 6, No 5, 74
 Soewadji Prawirohardjo (1939) *Geenesk Tijdschr Ned-Ind*, 79, 1691
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 Wheeler, C M (1938) *Amer J trop Med*, 18, 641
 Williamson, K B, and Zain, M (1937) *Trans R Soc trop Med Hyg*, 31, 111

ASCARIASIS

DIAGNOSIS

X-ray diagnosis

Chikiamco and Orquiza describe the roentgen diagnosis of ascariasis of the gastrointestinal tract. An X-ray plate exposed at from 4 to 6 hours after an opaque meal may display the ascaris as a cylindrical filling defect, as a string-like shadow thrown by the opaque substance which the parasite has swallowed, as 2 lines of shadow when it has clung to the cuticle of the worm or as a small polyp-like defect when the worm lies in the direction of the rays, but in children the diagnostic method fails, because they cannot swallow enough of the contrast substance.

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TREATMENT

Williams stated that oil of chenopodium provides the safest and most effective means of treating ascariasis in children, but that it is unsuitable for out-patient use. He suggested the following routine for an average child 3 years old. On the first day a fluid diet, containing plenty of glucose, is instituted, a mixture containing magnesium sulphate, 60 grains to the ounce, is given in doses of from $\frac{1}{4}$ to $\frac{1}{2}$ ounce, 3 times a day. On the second day, at 6 a.m., $\frac{1}{2}$ ounce of magnesium sulphate mixture is given, at 7 a.m. and again at 8 a.m., 6 minims of oil of chenopodium is administered, at 9 a.m. $\frac{1}{2}$ ounce of the magnesium sulphate mixture is again given, and repeated if the bowels have not acted at least twice after the last dose of chenopodium oil. On the third day, $\frac{1}{2}$ ounce of the magnesium sulphate mixture is given twice during the day.

- Chikiamco, P S, and Orquiza, C T (1940) *Acta med Philippina*, 2, 15
 Williams, C D (1938) *Arch Dis Childh*, 13, 235

ASPHYXIA IN CHILDREN

ASPHYXIA DURING THE EARLY WEEKS OF LIFE

Causes

Neonatal asphyxia

General review of neonatal asphyxia—Asphyxia neonatorum depends upon various factors, some of these antenatal and some postnatal. In the former group there are bad circulation in the mother, overdosage with drugs, excess of anaesthesia, toxæmia and placental abnormalities, in the latter group there are intracranial injuries at birth, premature birth and damage to viscera, there may also be suffocation as the result of inspiration of liquor amnii.

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Treatment—The infant body should be kept warm and an injection of $\frac{1}{1000}$ grain of atropine sulphate is advisable, this may be repeated. The mixture of oxygen and carbon dioxide may be demanded by circumstances, but artificial respiration should be conducted in very gentle fashion by pressure on the chest.

A rare cause of asphyxia in the new-born child is pneumo-mediastinum (Gumbiner and Cutler). In such cases the air may require aspiration.

Treatment

Special indications

It is now clearly established that respiratory movements occur in utero (Moncrieff), and American work shows that entrance of amniotic fluid into the lungs is a normal state of affairs up to the commencement of the later months of foetal life, when respiratory movements are inhibited but occur again in a marked manner if oxygen is cut off by pressure of the cord or after sensory stimuli. Therefore in resuscitation in addition to clearing fluid and debris from the respiratory tract it is important to clamp the cord and so stimulate breathing by cutting off the oxygen.

Gumbiner, B, and Cutler, M M (1941) *J Amer med Ass*, 117, 2050
Moncrieff, A (1940) *Practitioner*, 145, 244

ASTHMA

TREATMENT

Treatment of attacks

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In the words of Bray status asthmaticus still remains the *bête noire* of both practitioner and specialist as no single drug or procedure will at the same time lessen the spasm of the muscle, remove the oedema of the mucous membrane and ease the plugging and obstruction of the lumina of the bronchi

Hurst has made an extensive review of the situation especially as it affects children but has little to add to what is already common knowledge. He does not believe in 'asthma cures' and still thinks that much of the treatment of today is based on suggestion. Accordingly he states that the asthmatic can be taught a way of life and how to be happy in spite of the bad luck of having been born with the asthma diathesis

The following drugs have all been tried, some extensively, others with restricted application: adrenalin, ephedrine, aminophylline (a combination of theophylline with ethylene diamine), potassium salts, insulin, sodium phosphate, nicotinic acid, carbon dioxide (by inhalation), sulphonamides, amino-acids, anaesthetics, dilantin sodium, histamine. Not one of these drugs can be said to be specific for asthma, certainly in 2 cases in which for some reason the patient reacts with benefit to the remedy applied, the word success may be used. But status asthmaticus still remains as the demonstration of an intrinsic defect of the cellular physiology

Bray, G W (1943) *Practitioner*, 151, 210

Hurst, A (1943) *Brit med J*, 1, 403

ATHETOSIS

SIMPLE ATHETOSIS

Treatment

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Putnam has recorded the results of dividing the extra-pyramidal tracts in the spinal cord in patients with athetosis. Since 1931, 43 operations on 35 patients have been performed. There were 4 deaths, but 3 of these were among the early cases in the series and the mortality in the last 20 cases has been low. A large proportion of the patients showed improvement, having more control over their limbs and being able to do more for themselves, 4 patients were so much improved as to be able to seek employment

DOUBLE OR BILATERAL ATHETOSIS (ATHÉTOSE DOUBLE)

Clinical picture

Familial choreo-athetosis

A study which lasted for 2½ months at the Neurological Institute of New York of a man, aged 23 years, who since infancy had been subject to choreo-athetoid 'spells', confirms the basis of a record made by Mount and Reback, who stated that the condition, part of a familial paroxysmal choreo-athetosis, is a hitherto unrecognized syndrome. In 100 years there had been a family history of 20 cases in 5 generations, the condition originating in the great-grandfather. The authors concluded that the transmissibility was apparently a non-sex-linked recessive hereditary characteristic. On investigation it was found that the spells, which were roughly classified as small when they lasted for from 5 to 10 minutes and large when they lasted up to 2 hours, were prone to occur before, during or immediately after lunch. Alcohol had given rise to the spells on 3 occasions, always after the taking of about 2½ ounces of whisky. There was an aura consisting in a feeling of tiredness and in general tenderness in the chest and throat. Immediately afterwards one or both of the arms were simultaneously drawn up quickly, the arm being adducted at the shoulder and flexed at the elbow and wrist. Meanwhile there were slow athetotic movements of the fingers—irregular flexion, extension and spreading. There was diplopia and the foot on the affected side was supinated. When the major attacks or large spells held the patient, his speech was dysarthric and at times anarthric, but there was at no time any loss of consciousness. In many ways the condition resembled Huntington's chorea.

Mount, L. A, and Reback, S (1940) *Arch Neurol Psychiat*, Chicago, 44, 841

Putnam, T J (1939) *Yale J Biol Med*, 11, 459

ATHLETICS AND ATHLETIC INJURIES

ATHLETICS

Fatalities from exercise

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Jokl and Melzer have analysed a number of cases of acute non-traumatic collapse during work or sport. The results of necropsy were available in all, and in every

instance there was evidence of pathological conditions which were, in most cases, of long standing and of great severity, they included coronary arterial disease, aneurysm of the aorta, cerebral arterial disease, inflammatory disease of the heart muscle, degenerative disease of heart muscle, and rupture of the aorta or of the myocardium. Not one instance was recorded in which death could be regarded as due to the effects of extreme exertion on a previously healthy heart. In not a few instances the subjects had been entirely free from symptoms during life and had been capable of extreme exertion at least equal in severity to that which attended the fatal result.

The authors emphasize that effort carried to an extremity is incapable of causing injury when the myocardium is healthy and the cardiac reserve normal. They maintain that, to their knowledge, not a single fatal case of heatstroke in an athlete has yet been reported. This calamity is cited by Abrahams as the only serious potential risk to life in violent exercise in the case of the healthy. It is not suggested that its occurrence is other than rare, but it is undoubtedly a real danger if extreme exertion is carried out under conditions unfavourable to heat loss. A competitor in the Marathon race at Stockholm in 1912 who died on the road was regarded as an instance.

During the Olympic Games in Paris in 1924, the 6 miles cross-country race, a particularly exacting effort, took place on an exceptionally windless humid sultry day. There were no fatalities but several competitors collapsed with extremely alarming symptoms, even to the extent of coma, abolition of reflexes, and relaxation of sphincters.

Women and sport

Westmann, an obstetrician with personal experience of gymnastics and sports, regards competitive exercise as alien to the characteristics of the female constitution and as useless as well as harmful in relation to child-bearing. In his experience, many sportswomen have a flattened type of pelvis and he indicts excessive exercise as the cause of malformation. Menstrual disorders, especially dysmenorrhoea, are similarly attributed and uterine displacements are cited as following muscular strain. Ovarian deficiency and sterility with the production of the virago type is another consequence, and sports mistresses who succeed in becoming pregnant experience extremely difficult deliveries, especially during the stage of expulsion. Emotional storms have been encountered at the end of exhausting contests for which a relative instability of the endocrine system is blamed.

Whatever statistics have been obtained among women in Germany, these were not confirmed by a Committee appointed by the National Fitness Council to investigate such details in Great Britain. The Committee applied themselves to the investigation of such details as dysmenorrhoea, fertility, pregnancy, parturition, and various gynaecological as well as psychological details. The Committee interviewed many women who were prominent in the world of sport as active participants or as officials, and circulated a questionnaire to a large number of present and past participants and to a smaller number who had married and from whom details about child-bearing were obtained.

The activities of the Committee were interrupted by the outbreak of war but the Chairman pointed out that it was well to state provisionally that not a single example was forthcoming in which disadvantages of violent exercise were admitted or advanced. Many asserted that dysmenorrhoea, far from being made worse, was markedly improved since strenuous athletics had been undertaken.

There was no indication of relative sterility, of troublesome pregnancies, or of difficulties in delivery. On the psychological side, the matter might still be regarded as *sub judice*. The Committee added that, quite apart from the absolute antithesis of their results, they were not convinced by much of Westmann's thesis.

ATHLETIC INJURIES

Classification of injuries with their appropriate treatment

Joint injuries

Sprains—The use of procaine as an injection in the case of sprained joints has been recommended by Grieve. He gives from 1.5 to 2 cubic centimetres of a 1 per cent solution, this being injected into the area of maximum tenderness. On the relief of the pain another cubic centimetre is injected, sometimes it is advisable to give a third dose 24 hours later. Once the first injection has been given the injured joint should be exercised to the ordinary limits of movement and in all directions.

Ethyl chloride spray is in common use as a local anaesthetic in minor surgery. Its value for this purpose is doubtful, at the most it appears to deaden sensation. Recently this property has been used in minor orthopaedic cases to relieve muscle spasm and to numb sensitive areas sufficiently to enable simple manipulative treatment to be carried out, for example, in tennis elbow it is often difficult to obtain full extension of the elbow-joint because of spasm of the biceps, the taut tendon being very obvious in the antecubital fossa. If the area over the antecubital fossa and the common extensor origin is sprayed with ethyl chloride until 'frost' just begins to appear, it will be found that the spasm is inhibited for several minutes,

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during which time the joint can be put through a full range of movements. The increased range and absence of pain are very striking, and often make it possible to break down adhesions without discomfort. The advantage of being able to deal with small joints without a general anaesthetic is obvious, and the method deserves to be more widely known.

Recent articles have emphasized the therapeutic value of injections of local anaesthetics and of physiological saline in acute and chronic sprains. In acute sprains a tender point often corresponds with the torn fibres of some ligamentous structure, for example, below the external malleolus in sprains of the external lateral ligament of the ankle. Much of the immediate disability is due to reflex muscular spasm, and the injection of from 2 to 3 cubic centimetres of 1 per cent novocain (procaine hydrochloride) at the site of tenderness is often followed by striking relief for several hours. If this is supplemented by adequate physical treatment in the form of ionization, massage and faradic muscular contractions, all designed to promote absorption of exudate, the period of disability can be materially shortened.

In chronic cases organization of the exudations produces firm fibrotic areas in the tissues near the site of the injury. This fibrositis is often very resistant to treatment, and is responsible for much of the minor pain and discomfort described as muscular rheumatism. The injection of from 5 to 10 cubic centimetres of sterile physiological saline in conjunction with proper physical treatment produces striking results in many cases. The saline is injected into the substance of the fibrous mass, and its action is probably largely mechanical, breaking up the fibrotic masses and provoking reaction. The injection is painful and should be preceded by the injection of from 2 to 3 cubic centimetres of a local anaesthetic. In successful cases there is often a slight febrile reaction from 6 to 8 hours after the injection.

Abrahams, A. (1939) *Lancet*, 2, 309, 1091

Grieve, J. (1941) *Lancet*, 1, 344

Joki, E., and Melzer, L. (1940) *S Afr J med Sci*, 5, 4

Westmann, S. K. (1939) *Sport, Physical Training, and Womanhood*
London

AVIATION MEDICINE

GENERAL

Physiological considerations in aviation

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For the American Committee on Aviation a bibliography of some 6,000 items has been prepared by Fulton, who states that the performance of modern aircraft has now far outstripped the physiological limitations of the pilot. New problems depending upon the great heights to which airplanes can fly, upon the speed and range of modern bombers and upon other fundamentals have arisen—problems such as those of fatigue, stress and strain. One of the most important tasks before the medical profession is to try to accommodate the aviator to his ceiling. This means that anoxia must be counteracted by every possible method. It is an interesting fact that the cortex of the adrenal gland actively takes part in the reaction to anoxia. Such participation by the adrenal gland is emphasized by the fact that tired pilots after very high flights show signs of early Addison's disease.

In experiments on concussion by Denny-Brown and Russell, who have studied acceleration as well as deceleration, it is stated that the rate of acceleration necessary to cause concussion is as much as 46,000 feet per second, per second. So great may be the strain of the various manoeuvres of flying that the intervertebral disks may be ruptured.

SCHEME FOR THE EXAMINATION OF PILOTS

The flying temperament

The subject of mental aptitude for aviation was investigated in the Royal Air Force in 1918 by a Committee under the late W. H. R. Rivers, and for the information of those who are doing research into this particular subject it may be helpful if the recommendations which Rivers made on this subject are quoted.

(a) An investigation designed to discover whether it is possible to detect mental aptitude for the work of the Royal Air Force should be carried out on pupils before their admission to a flying school, and most appropriately at the school to which they go immediately after admission to the Force. (b) It is not enough to grade simply into classes according to general aptitude, but it is necessary to distinguish between such features as manipulative ability, fighting capacity, endurance, and intelligence. The following table illustrates the nature of the grading which is now being used at the 29th Training Squadron.

ABILITY	A	B	C	REMARKS
Manipulation	—			
Fighting	—			
Endurance	—			
Intelligence	—			

(c) Our work suggests that pilots who have the necessary interest in the subject will be the most suitable persons to act as examiners (d) The fatiguing nature of such examinations makes it quite impossible that they can form part of the general tests for admission to the R A F The existence of mental aptitude for flying is probably most important in borderline cases, among which the presence of definite aptitude might be allowed to counterbalance a degree of anatomical or physiological defect which would otherwise lead to rejection For this purpose special examiners might hold interviews in selected cases, or this inquiry might form part of the work of the assessors In general, however, inquiries into mental aptitude would come most appropriately at an early stage in training, and should be used as one of the means of excluding unsuitable candidates who have succeeded in obtaining admission to the R A F on the ground of physical and physiological suitability (Medical Research Council)

EXAMINATION OF THE SPECIAL SENSES

The eye

The examination of the eyes covers the following points (1) visual acuity, (2) colour vision, (3) visual judgment, and (4) fundi, fields, and external examination Visual acuity for permanent flying personnel in the Royal Air Force must reach 6/9 in each eye, provided that 6/6 can be obtained by correction and there is no suggestion of commencing myopia Temporary flying personnel are accepted with 6/12 vision in either eye so long as it can be improved to 6/6 by glasses For war-time piloting these standards have been relaxed, so that candidates can be accepted for piloting duties if they have a visual acuity of not less than 6/18 in either eye without glasses which is correctable to 6/6 in each eye with glasses Colour vision is tested by means of Ishihara plates, the Edridge-Green lantern, or preferably the Giles-Archer Colour Perception Unit There are three standards, namely (a) colour normal, (b) colour defective but safe, (c) colour defective and unsafe Those candidates who fall within the group covering the slight anomalous trichromats are placed in the second standard, i.e. colour defective but safe Such a scheme entails the rejection of less than half the number found to have defects of colour vision, yet ensures visual safety The ocular muscle balance is examined by means of the red-green and Maddox rod tests for distance, for near vision by the binocular gauge and Bishop Harman diaphragm tests Candidates with heterophoria which, in the opinion of the examining oculist, can be cured by means of suitable orthoptic exercises, can be accepted, and a course of visual training is given (Rook)

Ear, nose and throat

The ear, nose, and throat examination follows the usual routine The standard of hearing, ready perception of a forced whisper at 20 feet for each ear, still holds good, but the technique of the test has recently been modified and improved Normal hearing is necessary for every candidate for full flying duties or when the use of radio-telephony or wireless telephony is of paramount importance, as in the case of the wireless operator of an air crew (Rook)

The rotation test has been largely discontinued as a practical means of estimating vestibular sensitivity It has been found that the responses obtained in the rotation chair in no way predict the ultimate behaviour of a candidate in the air when subjected to aerobatics or other evolutions Detailed examination of the vestibular apparatus is carried out only in cases suggesting some pathological condition of the labyrinth (Bulletin of War Medicine)

Effect of flight on hearing

Campbell discusses the effect of flight on hearing, and the relation to age The author concludes, from a study of many hundreds of audiograms, that the effect of age usually becomes measurable after the second decade and is progressive both in degree and in frequency range Hereditary factors also influence the stability of the acoustic mechanism

SPECIAL TESTS FOR AEROBATICS

Air-sickness

Rippon has surveyed the problem of air-sickness from the point of view of the service pilot He emphasizes the importance of considering the functional efficiency of the individual as a whole when assessing fitness for flying duties He ascribes some symptoms to a mechanism of 'regression' This is the reaction of the organism when the higher centres of the central nervous system fail to adjust themselves to the abnormal conditions of flying, and, as the result, the physical reactions tend to correspond to those of a previous level or to revert to primitive reactions

Giddiness or vomiting in the air, and overaction of the circulatory system, are shown to be examples of regression with a release of the lower centres due to lack of control by the higher levels of the central nervous system The investigations of the late H Head on the sense of stability and balance in the air are described, and emphasis is laid on the observation that mental causes affecting consciousness adversely influence functional efficiency

For treatment of regressive states with impairment of flying efficiency, the value of a short course of psychotherapy prior to a period of sick-leave is emphasized

Bends

The condition known as 'bends' is one of pains in the limbs and the joints, sometimes with scotoma, nervous disturbances and loss of consciousness, and is the result of a discharge of nitrogen from its solution in the blood when the pilot flies above the 30,000 feet level. Bends have also been referred to as decompression sickness. The symptoms rapidly disappear when the aviator comes down to 24,000 feet. It is possible by certain tests to determine those who are susceptible and thus to prevent them from performing high altitude flights.

Blackening-out

The cause of the phenomenon of blackening-out is still unsettled. Rippon states that the principal factor is pooling of blood in the abdomen, resulting in cerebral anaemia. Rippon quotes a racing pilot who prevented blackening-out by taking and holding a deep breath when approaching a turn in a race and by contracting his muscles at the same time, he had developed his abdominal muscles till they resembled those of a boxer. Some pilots know what force they can stand without blackening-out. One member of a Schneider Trophy Team stated how many seconds he could stand 4g, and how many seconds 6g, above this it was possible to withstand the acceleration for only fractions of a second.

Livingston points out that the black-out point (4.5 to 7g) is now easily passed in modern aircraft and that the problem is therefore becoming more important. He states that the exact point in the visual apparatus that is primarily affected by the vascular disturbance is not known. He mentions 3 hypotheses: (1) that the visuo-cortical area is rendered temporarily insensitive to stimuli, (2) that there is a centrifugal stretching of the globe which affects the retina, and (3) that if the pressure in the retinal vessels is reduced by the centrifugal movement of the blood and the intra-ocular pressure remains constant, this might result in compression of the retinal vessels.

Hyperventilation

The hyperventilation syndrome is very important in aviation and a miniature reproduction of the condition may be obtained by a few minutes' voluntary forced breathing. Dizziness and faintness soon give way to numbness and tingling of the extremities, blurred vision and a clouded mentality. More important is the sense of alarm or apprehension. If the experiment is continued and the forced breathing is allowed to go on there may be indeed tetanic spasm of the muscles and particularly carpopedal spasm. There are also vasomotor disturbances with pallor, cyanosis, sweating and tachycardia and now and then a case may occur in which consciousness is lost.

The cause of the above condition is said to be due to the loss of an excessive amount of carbon dioxide from the blood so that the acid base equilibrium is disturbed, a condition of acapnia. Spontaneous hyperventilation in persons of normal emotional constitution may be part of an anxious state or a state of fear and it is easy to realize that aviators, especially when they are engaged in air combats, may suffer from hyperventilation. Hinshaw, Rushmer and Boothby carried out many investigations in connexion with hyperventilation, choosing 10 pilots at random and subjecting them to test. Two of the 10 partially lost consciousness and in the opinion of the observers were quite unfit in that state to control an airplane. Four others showed symptoms which were severe enough to have caused them considerable disability in flying. The others had negligible symptoms. An important finding was that the time taken to perform prescribed movements was increased by from 24 per cent to 41 per cent after hyperventilation.

LIST OF APPARATUS REQUIRED

Oxygen set

Boothby, Benson and Lovelace have devised an emergency oxygen set to help to ensure a safe escape and parachute descent from heights of about 20,000 feet and over. They state that if an aviator escaped from a plane at 35,000 feet and opened his parachute rapidly he would take about 10 minutes to reach 20,000 feet, by which time he would probably have died of anoxia.

- Boothby, W. M., Benson, O. O., Jun., and Lovelace, W. R. (1940) *J. Aviat. Med.*, 11, 59.
Bulletin of War Medicine (1941) 5, 337.
Campbell, P. A. (1942) *J. Aviat. Med.*, 13, 56.
Denny-Brown, D., and Russell, W. S. (1941) *Brain*, 64, 93.
Fulton, J. F. (1942) *New Engl. J. Med.*, 226, 873.
Hinshaw, H. C., Rushmer, R. F., and Boothby, W. M. (1943) *J. Aviat. Med.*, 14, 100.

BACKACHE AND LUMBAGO

- Livingston, P C (1940) Section 'Ophthalmology in Aviation', *Modern Trends in Ophthalmology* (Ridley, F, and Sorsby, A), p 624
London
Medical Research Council, *Special Report* (1920) Series 53, p 257
H M Stationery Office
Rippon, T S (1940) *Practitioner*, 144, 411

BACKACHE AND LUMBAGO

DIAGNOSIS

Extrinsic causes

Vol II, p 253 In paragraph 4 (*Backache following operations*), the last sentence should read Many an intractable case of backache might be avoided by the simple precaution of placing an air-cushion under the lumbar spine in order to support it during all abdominal operations, or by supporting the knee in a slight degree of flexion by a pillow

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Intrinsic causes

Bone disease

Vol II, p 254 To the second line from the foot of the page should be added Wide-field X-ray therapy also has a most beneficial effect on osteitis deformans

Joint disease

Vol II p 255 To the end of paragraph 3 (*Arthritis*) the following should be added It is an open question whether the changes often labelled arthritis are indeed worthy of that name Unfair wear and tear adds to the age, as it were, of any joint, and it would seem wise to consider many of the changes seen as due to arthrosis rather than arthritis The difference may be subtle but is of great importance in diagnosis and treatment Arthrosis is the result of trauma, and any unfair wear and tear traumatizes joints, arthritis is inflammatory

Vol II, p 256 To the end of the first paragraph, add the following If the inflammatory condition is the direct sequel to trauma, the more acute the condition the more urgently may manipulation treatment be necessary Expectant treatment may have disastrous results

Vol II, p 256 5 lines above heading (c), for 'Deep X-ray therapy' read 'Wide-field X-ray therapy'

Traumatic arthritis

Vol II, p 258 Paragraph 2 should read When standing the patient prefers to carry the weight on the leg of the uninjured side Stooping is far more limited than in the sitting position and the patient's trunk inclines towards the injured side

Vol II, p 258 10 lines from foot of page The new sentence should begin A little further out, immediately below the anterior superior spine

Vol II, p 259 Paragraph 2, lines 2 and 3, should read as follows it may be found that it is increased by pressing the anterior superior spine of the ilium backwards and upwards

Vol II, p 262 line 6 from foot of page The new sentence should read The band is most taut when the thigh is in the mid-position of rotation, for in this position it is held on stretch by the great trochanter

Vol II, p 263 line 15 The new sentence should read If the ilio-tibial band is unduly taut, and if the thighs are held down together, it will be impossible to raise the thigh on the affected side directly upwards so freely as on the sound side

Vol II, p 263 5 lines from foot of page After first word ('indicated') insert If the trauma is acute the patient may exhibit all the symptoms of an acute sciatic scoliosis

X-ray examination

Vol II, p 265 paragraph 6 Last sentence should read Again, with lumbarization of the first sacral there is a permanent tendency to instability of the sacro-iliac joint

TREATMENT

Vol II, p 266 For the second paragraph in this section substitute the following It is then necessary to decide which joint it is desired to move, and in which directions the movement is limited Finally the posture of the patient must be so arranged that all other joints are fixed by moving them to the extreme limit of anatomical movement, before any strain is laid upon the one joint which it is desired to move The essential point about the mobilizing force is that it must aim at moving one joint surface upon another It follows that one must be rigidly stabilized while the other is mobilized upon it A study of the living anatomy of the joints concerned is essential to success, not only to arrange for adequate fixation of the one bone, but to know exactly in which direction and to what extent the other is to be moved upon it Having decided these points, the law about the application of the mobilizing force may be summed up in the words 'pull' or 'press' To emphasize the nature of the force perhaps a better choice of words would be 'tug' or 'push',

There must be no element of jerk and the mobilizing force must be under perfect control, otherwise strain is inevitable. Whether it is possible to perform the necessary manipulation without an anaesthetic must depend upon the severity of the symptoms. It is hardly ever necessary to exert great physical force during any manipulation, beyond the force required to overcome the body weight of the patient. Provided it is clear what should be done, and given the knowledge of how to do it, the amount of physical energy expended should be very slight unless the patient is unduly tall or exceptionally heavy. Even so, the only force required is that which is sufficient to overcome the weight.

Novocain (procaine hydrochloride) injections

According to Burt there are 2 main groups of cases in which low back pain is predominant, one of these is due to the lesions in the deep structures of the back and buttock, known as Steindler's posterior division syndrome. The other is faulty posture, especially among schoolchildren (see below). Steindler has described 6 common sites for pain-producing lesions in the back and buttock, these being (1) at the insertion of sacrospinalis near the posterior or inferior iliac spine (sacrospinalis syndrome), (2) just over the lumbo-sacral joint (lumbo-sacral syndrome), (3) at the origin of the gluteus maximus just lateral to the sacro-iliac joint (gluteus syndrome), (4) at the articulation in cases of sacralized transverse processes (transverso-sacral syndrome), (5) at the upper part of the tensor fascia lata (tensor fascia lata syndrome), (6) in the substance of the erector spinae in the lumbar region (myofascial syndrome). He has special methods of diagnosis in which the suspected area is explored with a long needle and when a tender place is discovered a small amount of 2 per cent solution of novocain (procaine hydrochloride) is injected. Depending upon the reaction to the injection localization of the lesion can be made. The treatment is not easy and many difficulties arise because the patient frequently puts off going to the doctor and an important time is allowed to elapse between the onset of symptoms and the commencement of treatment. Functional considerations also weigh rather heavily in this type of case. If a case is brought under control early enough, however, ordinary physical treatment may have success but later manipulation may be essential and novocain injections especially are effective.

ABNORMALITIES

Spondylolisthesis

Vol II, p 272 The last paragraph of this section should read: Support is well-nigh impossible, and if, as so often happens, pain is disabling, there is no alternative to internal fixation. A posterior graft alone is often adequate.

POSTURAL DEFECTS

Vol II, p 273 lines 8 and 9 The sentence should read: There is usually a compensatory kyphotic curve above, but this is not always directly proportional to the extent of the lumbar curve.

Aetiology of faulty posture

Burt's second group of cases comprises conditions of bad posture. The latter has effect in 3 main ways: (1) it causes backache, (2) it leads to the production of back pain on account of other associated lesions, (3) it prolongs the time of recovery. Four main types of faulty posture are described, these being (1) the lordotic back, (2) the flat back, (3) the sway back and (4) the syndrome of the shop girl's hip. Examination should be carried out, especially among schoolchildren, to find out if there are any boys or girls who show tendencies to the development of postural backache. It is now the custom in certain professions, for example nursing, to have the entrant examined with regard to posture and in some hospitals regular re-examinations are carried out. After pregnancy postural backache may be a serious complication. The treatment of the established condition is by exercises and by massage or the application of heat.

THE LYMPHATICS AND FIBROUS TISSUE

Vol II, p 277 To the end of the first paragraph of this section add: In deeper structures we must include (d) those due to chronic strain or to injury.

Vol II, p 278 After paragraph 2 insert the following paragraph: (d) Sensitive deposits due to strain or injury may be found in almost any situation, but one example of each must suffice. When the ilio-tibial bands lack elasticity, the freedom of movement of the pelvis at the lumbo-sacral junction must be disturbed. Chronic strain is then laid upon the lowest interspinous ligament and this may not only become acutely sensitive, but also often from it pain will radiate to a considerable distance. A similar state of affairs may follow a sudden backward flexion combined with a twist—already mentioned as not uncommon in serving at lawn-tennis. The soft structures are nipped between the tips of two spinous processes and painful deposits are left at the site of trauma. Injection with procaine hydrochloride (novocain) and needling, as already described, will often suffice to remedy the complaint. In the lower back the muscles attached to the tips of the transverse

processes are often similarly affected, those of the first suffering more commonly than the others. Injection and needling is again the treatment best calculated to be effective.

Burt, H (1944) *Brit J phys Med NS*, 7, 11

BARTONELLOSIS

OROYA FEVER (GENERALIZED BARTONELLOSIS)

Infection by carriers

In the regions near Lima, Peru, in which bartonellosis is endemic an investigation was made of 230 persons by Howe, particularly with regard to immunology. The results of the researches were as follows. Sixteen showed established clinical evidence of bartonellosis and gave positive blood cultures, there was also a distinct rise in serum agglutinin titre while the disease ran its course. Nine patients had verruca peruviana with the blood cultures showing a higher average titre than those mentioned above. Six patients had signs of verruca peruviana with negative blood cultures, but the titre was high. There was a typical eruption and positive blood culture in 15 but agglutination was absent in the serum. Nine persons were symptomless but 8 of these gave positive blood cultures although one only showed agglutination, 3 of these had had a previous infection. Lastly there were 6 in whom neither history nor clinical evidence of bartonellosis could be made out, the blood cultures were negative but the agglutination tests were positive. The essence of this investigation is that as carriers were discovered by the methods described, such individuals may form a natural reservoir of infection.

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Prophylaxis

Since the wild sand-fly, *Phlebotomus verrucarum*, is the direct infecting agent and since this fly bites only at night, complete protection can be assured to inhabitants in endemic regions by leaving before nightfall the narrow strip of country between 800 and 3,000 metres above sea-level inhabited by the phlebotomus.

Howe, C (1943) *Arch intern Med*, 72, 147

BED-SORES

Addenda

In Vol II, p 305, after paragraph ending 'sometimes expedites healing' add 'Infrared radiation twice daily sometimes changes indolence into activity.'

On p 305, third paragraph in first sentence, after 'fractures' insert 'and severe wounds'. Delete 'of the limbs and spine'.

BERI-BERI

AETIOLOGY AND PATHOGENY

Vitamin deficiency

Pannekoek-Westenburg and van Veen, using Harris's bradycardia method in rats, have classified native foods into 3 categories, namely (1) those so rich in vitamin B₁ that they can be used to compensate for an otherwise deficient diet (husked rice, par-boiled rice, rice-bran, polishings of great millet, cassava leaves, peanuts, peanut-press-cake, and most of the seeds of the *Leguminosae*), (2) those containing an adequate but not excessive amount of vitamin B₁ (partly polished rice, Indian corn, great millet, fresh 'sweet' cassava, dried cassava skin, sweet potato, and potato), and (3) those containing but little vitamin B₁ (polished rice, glutinous rice, dried cassava root, dried cassava, gapelek flour, white bread, cow's milk, and soya milk). An important loss occurs in the decortication of grain, and, as there are no compensatory superlatively rich sources among the more commonly employed foodstuffs, it is probable that, under modern conditions, some degree of vitamin B₁ deficiency is extremely widespread.

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Most observers believe that little destruction of vitamin B₁ occurs in foodstuffs exposed to 100° C, but undue heat is undesirable and, as the vitamin is sensitive to alkalis, the addition of cooking soda to vegetables should be avoided. It is to some extent adsorbed on the starches, but it may be lost by solution in cooking, therefore cooking water and juices should not be discarded but should be incorporated into soups, sauces, or gravies.

Excess of pyruvate can be demonstrated in the blood in beri-beri, but this is only an expression of the disordered metabolism, since there is no evidence that injections of pyruvic acid are themselves toxic (Peters). The normal value for man's blood is between 0.4 and 0.6 milligram per 100 cubic centimetres of blood, the cerebrospinal fluid containing about half this amount, but, in fulminating beri-beri, values of over 1 milligram and even as high as 6 or 7 milligrams per 100 cubic centimetres of blood have been recorded. When no complicating factor is present these high values may be restored to normal in from 10 to 15 hours after the administration of 5 milligrams of vitamin B₁. Following muscular exercise a rise of blood pyruvate may be shown in the healthy person, but this rapidly returns to normal. In addition to the experiments with brain tissue it has been shown that the reduced oxygen uptake of kidney tissue from avitaminous pigeons can be restored to normal by vitamin B₁, this is of

interest in relation to the oedema of beri-beri, and it may be pointed out that avitaminous pigeons are in a state of latent oedema which can be made manifest by giving them salt. It has also been claimed, but not so clearly established, that vitamin B₁ exerts a similar effect upon the respiration of heart muscle.

In man the nervous phenomena are comparable to those in experimental animals. Jolliffe and his colleagues produced beri-beri experimentally in 4 out of 5 normal human volunteers. Symptoms were observed as early as the fourth day and signs as early as the fifth day, although one subject developed no symptoms or signs in 30 days on a diet estimated to contain only 62 per cent of his predicted minimal vitamin B₁ requirement. Symptoms observed were fatigue and lassitude, anorexia, precordial pain, burning of the feet, dyspnoea on exertion, muscle cramps, and palpitation. Signs were hyperaesthesia in sock distribution, changes in the electrocardiogram, and tenderness in the calf muscles. Addition of vitamin B₁ to the diets caused disappearance of symptoms in 3 days and of signs in 6 days. There was a good correlation between changes in the intake of the vitamin and its excretion in the urine, the urinary excretion being between 7 and 25 per cent of the intake.

A number of explanations have been advanced to explain the oedema of beri-beri. It may be dependent upon a specific effect of vitamin B₁, in the absence of which an intracellular oedema occurs, in some cases it results from cardiac failure or an increase in capillary pressure, in others it seems associated with a fall in the plasma proteins, and, finally, a functional failure of renal secretion, in turn influenced by the general cardiovascular derangement, may play some part. The association of muscular exercise is interesting, if the patient is disabled by the neuropathy, oedema is unlikely to develop, but, if muscular work is still possible, cardiac insufficiency and oedema will probably result (Keefer).

CLINICAL PICTURE

Classification of types

Acute pernicious or cardiac form

Acute cardiac failure may occur in beri-beri so suddenly as to constitute a real medical emergency and must not be overlooked when the majority of the cases of beri-beri are of the chronic form. In such cases the patients are breathless, restless and vomiting, the veins are engorged, there are cardiac dilatation, particularly right-sided, and moderate tachycardia, the diastolic pressure is invariably low, the pulse may be imperceptible and, without treatment, death occurs within a few hours. These moribund patients, after receiving an adequate amount, 5 milligrams or more, of pure vitamin B₁ intravenously, become less restless often within a few moments, after an hour or so the diastolic pressure begins to rise and the patient may even be able to get out of bed, within a few days the pulse slows, diuresis occurs, oedema lessens, and the patient is incredibly improved. The vitamin must be given in adequate amounts and injected intravenously to have any rapid effect, the reaction is quantitative, and, if insufficient vitamin is given, temporary amelioration may occur, but be followed by a sudden return of dyspnoea or collapse and death. The vitamin appears to be non-toxic and, although in these acute cases the systolic pressure rises with the diastolic, and the arteries feel increasingly rigid, the heart does not appear to labour. After a week this condition returns to normal, while, in normal persons and in cases of hypertension and chronic renal disease, no effect on blood pressure has been observed. In acute beri-beri the kidney frequently shows a functional insufficiency giving rise to scanty urine with albumin and casts, and a high blood urea which falls as the urine increases after treatment. Occasionally, when the fall in blood pressure has been so great that the kidneys have ceased to function, anuria may continue despite treatment with intravenous vitamin B₁ and death may occur from uraemia. For such cases Monteiro recommends calcium chloride 15 grains, glucose 1 drachm, water to 1 ounce, thrice daily, and intramuscular injections of 2 cubic centimetres of salyrgan.

Infantile beri-beri

According to Chan the common symptoms of beri-beri in infants are vomiting, sometimes severe, aphonia which is most striking, oedema mainly of the face and extremities and, in about 75 per cent of cases, loss of knee-jerks, more than 50 per cent of the cases show symptoms between the third and fourth weeks of life. More than half the number of mothers had signs of beri-beri, and in most instances there was a history of previous babies having died of a similar condition. With treatment consisting of replacing breast-feeding by the administration of vitamin B₁ extracts, the vomiting was the first symptom to disappear, and the aphonia the last. Mata also records good results from treating both infant and mother with synthetic vitamin B₁.

Clinical types — Earle contributes observations on infantile beri-beri and states that the constant signs of the chronic type are hepatic enlargement and hydrocele. The symptoms of the acute stage are (1) gastro-intestinal, (2) pneumonic or (3) those of meningismus with bulging of the fontanelle, head retraction and a pulse rate of 200

Treatment is symptomatic, with intramuscular injections of 1,000 units of vitamin B₁ given each day, sulphapyridine has given good results in cases of gastro-intestinal beri-beri

DIAGNOSIS

Meyers employs 2 clinical tests for beri-beri. The first is the development of a sound, audible with a stethoscope over the cubital fossa, following an injection of adrenaline. Sometimes in pronounced beri-beri such sounds are already audible over the large vessels before the injection of adrenaline but in these cases the injection emphasizes them.

The second and more important test depends on the diuresis following drinking 1 litre of water by the fasting patient. The diuresis is recorded half-hourly for 4 hours, by which time all the ingested water will have been excreted by a normal person, due allowance being made for sweating. In beri-beri, not only is there delayed excretion but, what is more significant, the excretion is restored to normal by administration of vitamin B₁ (Volhard's diuresis test).

Schretzenmayr showed by X-ray examination a rapid reduction in the size of the beri-beri heart, especially in its transverse diameter, following treatment with vitamin B₁ and suggests that this may be of great value in differential diagnosis.

Chan, M (1935) *Chin med J*, **49**, 676

Earle, K V (1941) *J trop Med (Hyg)*, **44**, 142

Jolliffe, N, Goodhart, R, Gennis, J, and Cline, J K (1939) *Amer J med Sci*, **198**, 198

Keefer, C S (1930) *Arch intern Med*, **45**, 1

Mata, C (1939) *J P I med Ass*, **19**, 493

Meyers, F M (1938) *Geneesk Tydschr Ned-Ind*, **78**, 1537

Monteiro, E S (1939) *J Malaya Br Brit med Ass*, **3**, 177

Pannekoek-Westenburg, S J E, and van Veen, A G (1939) *Geneesk Tydschr Ned-Ind*, **79**, 2891

Peters, R A (1938) *Trans R Soc trop Med Hyg*, **31**, 483

Schretzenmayr, A (1939) *Arch Schiffs- u Tropenhyg*, **43**, 427

BLACKWATER FEVER

PATHOLOGY

Pathogenesis

Although the fundamental pathological process in blackwater fever still remains unknown, much has been done within the last decade to clear up details of the mechanism involved. Among recent observations may be mentioned those of Foy, Kondi and Moumjidis on the behaviour of normal blood after transfusion in cases of blackwater fever, and contrariwise of blackwater fever blood after transfusion into patients in non-blackwater fever cases. After a transfusion of 25 cubic centimetres of blackwater fever blood (return flow at end of transfusion) the result in a normal person was, as is now to be expected, a subsequent attack of *falciparum* fever, showing that the blackwater patient had circulating malarial parasites in the blood, there was not any blackwater fever or haemoglobinuria. The contrary result was more informative. Three patients with blackwater fever were given transfusions of normal blood, all showed rapid haemolysis of the transfused cells, which indicates that normal cells introduced into the circulation of patients with blackwater fever are haemolysed, and therefore that the essential condition in this disease does not lie in a special fragility or weakness of the erythrocytes themselves.

Observations by Vint and others on the structure and behaviour of the exposed transilluminated spleen of laboratory animals also have a distinct bearing on the possible mechanism of blood destruction in blackwater fever. The observers summarize what is known of the spleen structure. Knisely observed the exposed transilluminated spleens of mice, rats and cats. He found, contrary to previous ideas held, that the arterial blood vessels were continuous without any blind ends and did not terminate blindly in the pulp. The blood passes by long straight capillaries to the venous sinuses, its flow being controlled by sphincter-like segments of the arterial tree. When the efferent end of the venous sinus contracts tightly the sinus fills. The plasma filters out through the fenestrae in the walls, leaving the erythrocytes behind. This process continues until the sinus is distended from 20 to 50 times its normal size with tightly packed erythrocytes. The plasma returns to the circulation through the stigmata in the walls of the venules but the blood corpuscles may remain packed in the sinus for periods of from 10 minutes to several hours, then the efferent end of the sinus suddenly opens and the packed cells are discharged in masses. When the sinus has returned to its normal size blood is conducted as in an ordinary blood vessel. This explains what Barcroft found, namely that the spleen, although only 0.25 per cent of the body weight, could yet add 100 cubic centimetres of corpuscles to the circulation.

If citrated or defibrinated blood is kept at body temperature it undergoes *rouleau*

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formation and sedimentation. If the sedimented blood is shaken up the sedimentation rate is reduced, *rouleau* formation is diminished and the erythrocytes tend to become globular (stabilization). Blood cells held up in the venous sinuses of the spleen may therefore, in the blackwater fever condition, have become abnormally vulnerable and undergo haemolysis when reintroduced into the blood stream. Some such process may well occur in blackwater fever although the nature of the change undergone by the cells, or the reasons for this, remains undisclosed.

Pathology of blood and urine

Fairley's classification of pigments present in the organs and tissues of the body is as follows: (1) Visceral pigments (a) Malarial pigment or haemozoin does not give the Prussian blue reaction, occurs in cells of the reticulo-endothelial system as brownish-black granules or clumps of black pigment, is present in small quantities in blackwater fever but, apart from malaria, is seen in only one other disease, namely bilharziasis, in which it is formed from partly digested blood regurgitated into the area of the portal vein by the worms, is similar to, if not identical with, haem or haematin (b) Haemosiderin normally a fine brown pigment in the parenchymatous cells of the liver, spleen and kidneys, is greatly increased in blackwater fever and other diseases characterized by considerable haemolysis (2) Plasma pigments (a) Oxyhaemoglobin (b) Pseudo-methaemoglobin (c) Bilirubin, hyperbilirubinaemia is seen in all severe cases of blackwater fever (3) Biliary and faecal pigments formed as a direct result of increase in haemobilirubin (4) Urinary pigments (a) Oxyhaemoglobin (b) Methaemoglobin (c) Urobilin (d) Brown pigment, found as deposit in blackwater fever urine and blocking tubules of kidney, generally considered to be acid haematin.

Further knowledge of the nature and significance of pseudo-methaemoglobin has resulted from researches by its discoverers and others. It is known to be produced when methaemoglobin, sulphaemoglobin, haematin, or alkaline solution of pure haem is incubated with human plasma at 40° C. The change is produced with both human and monkey serums but not with rabbit or guinea-pig serum. In the body it is formed from extracorporeal haemoglobin whenever blood is destroyed in large quantities and the haemoglobin remains in the circulation for a sufficient length of time. It has been demonstrated by Fairley and Bromfield^{1, 2} in pancreatic cyst fluid and also in nocturnal haemoglobinuria (Marchiafava-Micheli syndrome) and in incompatible blood transfusion. The pigment may presumably be expected whenever the conditions noted above are complied with.

Pseudo-methaemoglobin, now termed more correctly methaemalbumin, may be produced, as proved by experiments, in the following way. First, neutral or alkaline methaemoglobin is formed, this is then split into globin and haematin (ferric). The latter joins with serum albumin to form methaemalbumin (Fairley).

Barcroft, J (1925) *Lancet*, 1, 319 *The Respiratory Function of the Blood* Part 1, London, p. 171

Fairley, N. H. (1941) *Quart. J. Med. N.S.*, 10, 95, 115

— and Bromfield, R. J. (1938)¹ *Trans. R. Soc. trop. Med. Hyg.*, 31, 374

— — (1939)² *ibid.*, 32, 431

Foy, H., Kondi, A., and Moumjidis, A. (1941) *Trans. R. Soc. trop. Med. Hyg.*, 35, 119

Knisely, M. H. (1934) *Proc. Soc. exp. Biol.*, N.Y., 32, 212

Vint, F. W. (1941) *E. Afr. med. J.*, 18, 162

BLADDER DISEASES

NEOPLASMS

Hunner's ulcer of the bladder

Clinical picture and diagnosis

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This condition, which is commonly referred to as panmural fibrosis, is a myositic ulcer which occurs in the dome or vertex of the bladder wall. The outstanding symptom is frequency of micturition which is present all through the 24 hours, so greatly is this pathognomonic of Hunner's ulcer that if the patient does not complain of nocturnal frequency then the case is emphatically not one of Hunner's ulcer. There is also suprapubic pain, haematuria in 60 per cent and pyuria in 60 per cent of patients. Ninety per cent of those affected are females and the average age is 48 years. In examination with a cystoscope the ulcer may be somewhat elusive as bladder distension gives rise to severe pain. If a spinal anaesthetic is given and the cystoscope inserted, a careful search may result in the discovery of the ulcer in the dome of the bladder, the surface of the ulcer being formed of granulation tissue which bleeds very quickly. The rest of the bladder lining is clean and free from phosphatic deposits. There may be several discrete areas of ulceration.

Treatment

The work of Pool and Crenshaw depends upon the application of a 1 in 5,000

solution of silver nitrate The bladder should be well irrigated and 2 or 3 ounces of the solution left in for 5 minutes The catheter is then passed and the remaining silver nitrate is drawn off Ultimately the strength of the solution of silver nitrate may be raised to 1 in 100 Methyl violet has also been used and in extreme cases the operation of transplantation of the ureters into the intestine may be resorted to In mild cases distension at intervals may help to heal the ulcer

TUBERCULOSIS

Treatment*Advanced tuberculosis*

As an addition to what has been said in the *Encyclopaedia* (Vol II, pp 390-3) about tuberculosis of the bladder, the description of the severe case may be amplified, and the treatment summarized, from the active surgical viewpoint Drugs may be expected to have failed and sympathectomy is not a reliable operation The operations of nephrostomy, uretero-enterostomy and cutaneous ureterostomy must be considered and the one chosen most suitable to the case under review The first indeed may be ruled out because it is best to have the urine prevented from reaching the bladder The second method may therefore be most suitable The disadvantages are that it has a very high death rate because the patient is generally in an advanced state of the disease The remaining or third method is therefore most commonly adopted The ureter is reached by an incision made in the iliac region and after the vesicular end has been clamped, divided and carbolized, it is brought to the surface, all tension and angulation being avoided The wound is closed round the exposed ureter which protrudes for a few centimetres from the sutured area The ureter is not anchored in any way, because an essential is that it should have freedom and that there should not be any constriction of blood vessels or of the tube, it is fixed to the edges of the skin incision and thus an artificial outlet is provided Meanwhile a rubber catheter is passed into the pelvis of the kidney and the urine is drawn off by this method until the abdominal wound is healed Thereafter treatment can be carried out by constant catheterization or else by the wearing of a urine bag similar to a colostomy apparatus

Pool, T L, and Crenshaw, J L (1941) *Proc Mayo Clin*, 16, 718

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BLINDNESS

TRAUMA

Injuries to cornea, sclera, lens and uvea*Cornea*

In some cases of chemical or thermal burns of the conjunctiva in which the tissues are considerably damaged the subsequent corneal opacification may be prevented or considerably reduced by excision of the injured conjunctiva and episclera down to the sclera and as far as the corneo-scleral junction The raw area is covered by a sliding graft of adjacent conjunctiva whenever this is possible or by a mucous membrane graft taken from the mouth and sutured in position

Sympathetic ophthalmitis*Symptoms*

Vol II, p 415, lines 19 and 20 The sentence should now read Slight ciliary injection and tenderness, lachrymation, punctate precipitates on the posterior surface of the cornea and vitreous opacities are important physical signs

Trauma of lens and vitreous*Other causes of cataract*

Vol II, p 417, line 7 The end of the sentence should read varying from 9 months to 8 years

Trauma of retina*Detachment of retina*

Treatment—Vol II, p 419, lines 1-8 (See also Vol X, p 636) Substitute the sentence beginning 'A current of 65 to 70 milliamperes' by the following A current of from 70 to 120 milliamperes for 7 seconds is used The amount of current varies with the body resistance of different patients, and it should be assessed during operation by ophthalmoscopic examination after each application A greyish-white area of coagulation about 3.5 millimetres in diameter should be seen in the choroid and retina around the site of the retinal tear When circumvallation of the edges of the retinal tear has been thoroughly effected perforating diathermy is employed The length of the needle varies from 1 to 2.5 millimetres and depends upon the depth of the detachment and the thickness of the sclera over the site of the retinal tear The object is to press the tip of the needle into the retina around the edge of the tear and at the same time to allow the interretinal fluid collected between the layer of rods and cones and the retinal pigment epithelium to seep through the sclera and drain away The punctures are made through the sites of the surface diathermy applications and the current should be 40 milliamperes for 3 seconds Drainage of the interretinal fluid is completed by suction applied over the perfora-

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tions in the sclera. Any divided muscle is sutured with mattress stitches and the wound in the conjunctiva is closed. The patient is nursed so that the site of the retinal hole is in the most dependent position which it is possible to attain. The head is secured thus between sandbags or by means of a restraining bandage applied lightly across the forehead.

Other types of trauma

Gases

Vol II, p 419, paragraph 7 should read: In chemical warfare a drop of mustard oil as small as 0.004 cubic centimetre produces a severe keratitis and corneal necrosis. Secondary infection by pyogenic micro-organisms may lead to serious impairment of vision and in many cases loss of the eye from panophthalmitis. Mustard vapour in concentrations higher than 1 in 10,000,000 produces serious corneal complications when the exposure to the gas is of some duration in soldiers, who become more susceptible to its cumulative action from previous exposures. Ten years or more after the corneal inflammation and ulceration have healed such lesions recur. The corneal sensitivity is reduced, the conjunctival vessels in a zone about 3 millimetres wide around the corneo-scleral junction are tortuous, varicose, and set in a dense subconjunctival fibrous tissue matrix. The appearance is characteristic. The first-aid treatment of mustard burns of the eyes consists of copious lavage with lukewarm sodium bicarbonate 3 per cent, care being taken not to direct the stream at the cornea. Cod-liver oil drops may be instilled, the vitamin A content of these may exert a good effect on regeneration of the epithelium. It is improbable that the oil has any solvent effect on the mustard, which is combined with the tissues completely within 15 minutes of the injury, conjunctival secretions from affected eyes instilled into the eye of an experimental animal after this time produce no reaction. Pantocaine (butethanol, tetracaine, anethaine, decicain), or *p*-butylaminobenzoylethylmethylaminoethanol hydrochloride, 1 per cent, a local anaesthetic, may be used to relieve pain. Cocaine should never be employed and the eyes should not be bandaged. Albucid (sulphonamide) drops 2.5 per cent are under trial and together with sulphonamides by the mouth are alleged to reduce the degree of secondary infection in experimental animals. Dark glasses should be worn. The patients injured by vapour should be assured that they are able to see objects by removing the discharge from the lid margins and opening their eyes. Tarsorrhaphy (temporary suturing of the eyelids) should be done in some cases. After mustard-gas injuries neurasthenia commonly follows and should be dealt with by gradual occupational therapy and by placing the patients in surroundings in which a spirit of optimism and hope abounds. When sequelae take place some years after the original injury has healed contact glasses reduce the incidence of recurrent keratitis and corneal ulceration, render the eyes more comfortable, and improve vision by correcting the irregular astigmatism. Keratitis has also been reported after exposure to sewer gas.

Radium

Vol II, p 419, paragraph 8 should read: Radium, applied in massive doses near the eye, has been responsible for corneal necrosis. Cataract, retinal exudates around the macula, and optic atrophy have also followed the employment of large doses of radium.

INFLAMMATION

Inflammation of conjunctiva

Ophthalmia neonatorum

152 *Prophylaxis*—Vol II, p 421, lines 4–6. Substitute the sentence beginning 'One drop' by the following: One drop of 1 per cent fresh silver nitrate solution should be instilled into the conjunctival sacs if there is any suspicion of infection in the maternal passages.

Vol II, p 421, paragraph 3. In the second sentence substitute 'injected' for 'infected'.

Treatment—Vol II, p 421. At the end of paragraph 5 insert the following: The administration of sulphonamides, sulphapyridine for gonococcal and pneumococcal conjunctivitis, and sulphathiazole for streptococcal and *B. coli* infections is followed by remarkably good results. In many instances when this treatment is begun early in the course of the disease, corneal and intra-ocular complications do not occur and the duration of the disease is reduced from an average of 21 days to 7–9 days. Within 48 hours from the beginning of treatment the conjunctival discharge is considerably less, and cultures on the third and fourth days may reveal no bacteria. All signs of the disease have generally disappeared by the seventh day.

Purulent conjunctivitis in adults—Vol II, p 421, paragraph 7. In the second sentence substitute '(2 per cent)' for '(1 per cent)'. At the end of the paragraph add: Sulphapyridine should be administered by the mouth.

Trachoma

Aetiology—Vol II, p 422, paragraph 2 should read: The aetiology of trachoma is obscure. Research work is now directed towards isolation of a virus, which appears to be transmissible through the bodies of lice.

Treatment—Sulphanilamide therapy maintained at a blood concentration of from 5–10 milligrams per 100 cubic centimetres of blood for from 10–14 days has a favourable effect. By the 3rd day inclusion bodies disappear from the conjunctival epithelial cells, photophobia clears up in 24 hours, conjunctival discharge ceases and the relatively avascular lymphoid follicles either persist or are only partially absorbed, but do not give rise to symptoms.

Pemphigus

Vol II, p 422, at the end of paragraph 5 the following should be added. Contact glasses filled with liquid paraffin in the form of paroline afford some relief and improve vision slightly.

Ulceration of cornea keratitis

Interstitial keratitis

Treatment—Vol II, p 424. The following should be inserted at the end of paragraph 6. In some cases pain is very severe and is accompanied by intense blepharospasm and photophobia. It is quite unrelieved by heat and hypnotics. The retro-ocular injection of 2 cubic centimetres of novocain, 2 per cent, followed 7 minutes later by 1 cubic centimetre of alcohol, 40 per cent, is made into the region of the ciliary ganglion. Pain, photophobia and blepharospasm disappear. In some cases it is necessary to repeat the treatment in 2 weeks.

Inflammation of the optic nerve

Optic neuritis

Symptoms—Vol II, p 427, paragraph 6. At the end of the third sentence 'and medially' should be added.

Panophthalmitis

Treatment—Vol II, p 429, paragraph 5. Between the first and second sentence read: Sulphonamides are worth trying in the early stages.

TUMOURS

Sarcoma of the uveal tract

Treatment—Vol II, p 431, paragraph 3. The third sentence should read: The suturing of radon seeds to the sclera over its site is worth a trial when the affected eye is the only one remaining and if some healthy retina is still present.

153

Angiomatosis retinae (von Hippel-Lindau's disease)

Vol II, p 432. At the end of paragraph 4, after 'other viscera', the following should be added: The ocular lesions may precede those by 10 to 15 years.

Treatment—Vol II, p 432. The fifth paragraph should read: In the early stages the growth of an affected area in the retina may be arrested by electrolysis. The needle is passed through the sclera into the lesion. The effect is checked by ophthalmoscopic examination during operation.

VASCULAR AND BLOOD DISEASES

Embolism and thrombosis

Obstruction of central retinal artery

Treatment—Vol II, p 438. At the end of the fourth paragraph the following should be added: Retro-ocular injection of acetylcholine into Tenon's capsule is worth a trial for its vasodilator effect.

155

Thrombosis of central retinal vein

Treatment—Vol II, p 438, paragraph 8. At the end of the first sentence the following should be added: The administration of heparin intravenously is *sub judice*.

REFRACTIVE ERRORS

Treatment—Vol II, p 445, paragraph 2. The eighth sentence should read: This method is designed to produce choroiditis over the site of the retinal tear and, after drainage of the interretinal (subretinal) fluid through scleral punctures made with a perforating diathermy needle, to establish choroido-retinal adhesions, and by occluding the retinal tear to prevent the passage of fluid from the vitreous into the interretinal space.

158

GLAUCOMA

Primary glaucoma

Treatment—Vol II, p 447, paragraph 2. The fourth sentence should read: Six ounces of magnesium sulphate, 50 per cent, administered by the rectum will reduce the intra-ocular pressure for 24 hours or so.

159

CATARACT

Other causes of cataract

X-rays and radium—Vol II, p 451, paragraph 2. The first sentence should read: Posterior cortical opacities also occur from 9 months to 8 years after exposure of the region of the eye to X-rays or radium.

160

Dinitrophenol—Vol II, p 451. The following should be added to the end of paragraph 2: Dinitrophenol taken internally for the purpose of slimming has produced bilateral cataract of rapid progress, becoming mature in 6 months. The lens

- 160 becomes swollen and has a characteristic dense milky colour. Visual acuity is restored by removal of the cataract. Cataract has also been noted in persons who have taken moderate doses of thyroid extract for the purpose of weight reduction.

POISONS

- 162 *Tobacco*—Vol II, p 452. At the end of paragraph 3 the following should be added: Subcutaneous injections of acetylcholine and intravenous vasodilators are under trial. There is clinical evidence that visual recovery is accelerated by these substances.
Methyl alcohol—Vol II, p 452. Between paragraphs 7 and 8 the following should be inserted: Lumbar puncture is recommended immediately the diagnosis is made.

BLOOD EXAMINATION

CELLULAR CHANGES

Determination of corpuscular volume

- 163 For the determination of corpuscular volume and for other haematological procedures, Wintrobe recommended 4 milligrams of potassium oxalate and 6 milligrams of ammonium oxalate per 5 cubic centimetre tube. The tubes were prepared by measuring 0.2 cubic centimetre of a solution containing 2 per cent potassium oxalate and 3 per cent ammonium oxalate into the 5 cubic centimetre tube and evaporating to dryness in an incubator. Waxed corks or rubber bungs were essential in order to prevent absorption of plasma.

Relations between red-cell count, haemoglobin content and red-cell size

Mean corpuscular average thickness

In certain morbid conditions the normal relation between the volume, the diameter and the thickness of the erythrocyte is altered. In obstructive jaundice the diameter increases at the expense of the thickness, so that the cell becomes flatter than normal, whereas in acholuric jaundice, particularly the congenital type, the reverse takes place and the cell becomes more globular (spherocytosis). The phenomenon of spherocytosis is detected by correlating the mean corpuscular volume (see Vol II, p 474) with the mean corpuscular diameter (see Vol II, p 479) and calculating the mean corpuscular average thickness. This is accomplished by assuming that the red corpuscle has the form of a cylinder of known volume and known diameter, from which the height (thickness) can be calculated. The formula for calculation is as follows:

$$\text{Mean corpuscular average thickness in microns} = \frac{\text{Mean corpuscular volume}}{\pi \left(\frac{\text{Mean corpuscular diameter}}{2} \right)^2}$$

The normal range is from 1.7 to 2.5 μ .

The relation between diameter and thickness can better be appreciated by the diameter-thickness ratio, which is normally from 2.4 to 4.2. Ratios lower than 2.4 indicate spherocytosis.

Examination of bone marrow

In certain anaemic states the peripheral blood may not show diagnostic changes and a proper opinion cannot be given without an examination of the bone marrow. The procedure is not required as a routine but is often essential in aleukaemic leukaemia (see Vol VIII, p 36), aplastic anaemia, carcinomatosis of bones, myeloma, myelosclerosis and achrestic anaemia. Bone marrow examination is also useful for the diagnosis of latent forms of malaria and kala-azar, in which field it has largely replaced splenic puncture. The sternum is the most convenient bone. The marrow may be obtained by needle puncture, the material then being examined as a smear, or with a small 1 cubic centimetre trephine, the specimen being fixed and examined as a histological section. Sections are essential for the diagnosis of myelosclerosis and usually for aplastic anaemia.

The technique of sternal puncture is as follows. One hour before operation the patient should receive aspirin, 10 grains, and nepenthe, 15 minims. With the patient lying on his back, the skin, subcutaneous tissues, and periosteum over the sternum, at the level of the second interspace, are infiltrated with a small quantity of 2 per cent procaine hydrochloride (novocain). A Salath needle, previously sterilized in hot oil, is pushed through the skin to the bone, the stop being set at from $\frac{1}{4}$ to $\frac{1}{2}$ inch above the skin level. The needle is then driven through the outer table of the sternum by sharp taps from a small hammer, a definite 'give' is felt as the needle enters the marrow cavity. The stylet is removed and a dry 1 cubic centimetre syringe attached and gentle suction applied, a characteristic suction pain occurs if the needle is in the proper place. Marrow fluid to the amount of 0.25 cubic centimetre is withdrawn and is mixed in a tube with oxalate mixture. No more than this amount should be aspirated, because removal of larger quantities causes severe pain. The oxalate mixture is the residue from evaporation in an incubator of 0.1 cubic centimetre of a solution containing 0.2 per cent potassium oxalate and 0.3 per cent ammonium oxalate. Smears are made from the oxalated fluid within half an hour of collection.

A total nucleated-cell count is carried out in a counting chamber, diluting with leucocyte fluid in an erythrocyte pipette at 1 in 200, or in a leucocyte pipette at 1 in 20, according to the number of cells. Films are stained with Leishman's stain, and a differential count of 400 cells is made.

COAGULATION (BLOOD PLATELETS)

164

In the normal person the platelets in circulation number from 250,000 to 500,000 per cubic millimetre, but there are rapidly alternating periods when platelets are found in large numbers and when they are scanty. It is generally acknowledged that platelets are concerned with 3 processes, namely coagulation, clot retraction and adherence to the wall of a damaged blood-vessel for the purpose of temporary repair.

With regard to coagulation, platelets are an important source of thrombokinase or cephaline which, in conjunction with free calcium-ions, activates prothrombin to form thrombin which then interacts with fibrinogen to form fibrin. Comparatively small numbers of platelets will bring about coagulation, and another source of thrombokinase, namely damaged tissue cells, contributes to clot formation. The characteristic feature of platelet deficiency is not therefore a prolongation of coagulation time, the result of deficiency is more clearly shown by an interference with the other two functions of platelets. Thus the clot formed is soft and friable, for it lacks the presence of sufficient platelets which ordinarily form nodal points for strengthening the fibrin network, the bleeding time is prolonged because it takes time for a sufficient number of platelets to adhere to the damaged vessel-wall and stop the leak. There is also a great tendency to capillary haemorrhage, either spontaneous or as the result of slight trauma, or from pressure such as is applied in Hess's capillary-resistance test.

As a general rule spontaneous capillary haemorrhage does not occur until the platelet count is below the critical level of 40,000 per cubic millimetre. With the possible exception of essential thrombocytopenic purpura haemorrhagica, it is generally acknowledged that mere lack of platelets is not in itself sufficient to account for the occurrence of purpura. There is usually some additional factor which causes damage to the capillary endothelium. This additional factor may be an inherently defective capillary wall or an endothelium damaged by bacterial or virus toxins, poisonous drugs, under-nutrition, or lack of a specific factor, for example vitamin C. In practice endothelial damage is a much more common cause of purpura than is a deficiency of platelets. Essential thrombocytopenic purpura haemorrhagica is almost the only haemorrhagic disease in which a reduction in platelets is constant and consistent.

From the opposite aspect it is considered that an excess of platelets implies a liability to thrombosis. Operative procedures, particularly splenectomy, lead to a vast increase in circulating platelets, and this undoubtedly contributes to the causation of post-operative thrombosis, but here again the condition of the vascular endothelium is an important determining factor. It has been suggested that in haemophilia the platelets are unduly stable but it is highly improbable that this is the sole cause of the disease. Tocantins has reviewed the whole subject of the mammalian platelet in health and in disease.

Prothrombin content of blood

The principle of the method of Quick, Stanley-Brown and Bancroft is to mix optimal amounts of all the substances required for coagulation with the exception of prothrombin. These substances consist of thrombokinase or tissue extract, calcium and fibrinogen. The coagulation time of the mixture is then inversely proportional to the amount of prothrombin present. The test is mainly performed as a pre-operative measure in cases of jaundice. The oxalated blood (4.5 cubic centimetres venous blood to 0.5 cubic centimetres M/10 solution of sodium oxalate) which is used for the estimation is recalcified at the time of the test by adding calcium chloride. Thrombokinase is made from brain tissue obtained from a post-mortem room, this is freed from meninges and blood vessels, washed to remove all blood and then pulped and ground into a paste, it is then spread as a thin layer on sheets of glass and dried with a hot air electric blower. The dried brain is stored in a well-stoppered bottle. Immediately before use 2 grammes of the dried brain is emulsified in 10 cubic centimetres of physiological saline, incubated for 15 minutes at 37° C and afterwards filtered through gauze. For the estimation, 0.1 cubic centimetre of oxalated blood plasma and 0.1 cubic centimetre of the filtered brain emulsion are placed in a clean dry test-tube, taking the time with a stop-watch, 0.1 cubic centimetre of M/40 CaCl₂ in distilled water is added and the tube immersed immediately in a water bath of 37° C, being shaken vigorously at first and then rocked gently until coagulation occurs. The time from the moment of adding the calcium salt to the occurrence of coagulation is the *prothrombin time* which should be expressed as a percentage of increase over a normal control plasma test performed at the same time.

Bleeding time

A sphygmomanometer cuff is placed on the arm and the pressure raised to 40 milli-

- 164 metres in order to cut off the venous return, the pronator surface of the forearm is then punctured in 3 places with a stylet to a depth of 2.5 millimetres and the blood absorbed on blotting paper, as in Duke's method (see Vol II, p 483), 3 punctures are made in order to obtain an average. The maximal normal bleeding time by this method is 240 seconds, but it rarely exceeds 180 seconds (Ivy, Shapiro and Melnick)

SEROLOGICAL TESTS

Haemagglutination

The Rh factor

- 166 Much research has been done in recent years with regard to the part played by the agglutinin present in human blood which reacts with anti-Rh serums and with human iso-antibodies. The Rh factor, as it is called, has considerably revolutionized many activities associated with blood transfusion and similar procedures. It is known that 85 per cent of the white race harbour this factor. If immune iso-antibody is formed there may be alarming reactions when blood is transfused. Many tests have been devised and many adjustments decided upon with regard to blood transfusion and the presence of the factor can be determined by these certain methods. Landsteiner, Wiener and Matson have compared the properties in the blood of American Indians and of the white population of New York. So far as New York is concerned it has about the average (85 per cent) of Rh positive individuals. In American Indians less than 1 per cent are Rh positive.

Agglutination tests

Glandular fever (Paul and Bunnell test)

This diagnostic test for infectious mononucleosis is based on the accidental discovery that blood serum contains heterophil antibodies in the form of an agglutinin for sheep's erythrocytes. The agglutinin is usually sufficiently strong to be diagnostic by the fourth day of the disease, and it is present in high titre during the active phase. The reaction is apparently specific for glandular fever with the single exception of serum sickness, especially recent serum sickness. The agglutinin differs from the 'cold' agglutinin for sheep's cells, sometimes found in normal blood, in that it is usually active at 37° C and 5° C.

There are several methods of performing the test. Variations are confined mainly to the amount of serum used and to the strength of the suspension of sheep's cells. In all methods it is essential first to inactivate the serum by heating for from 20 to 30 minutes at 55° C and to use sheep's cells that are not less than 24 hours old and not more than 5 days old, the cells must be freshly washed on the day of the test. A saline control must always be included in the test.

PHYSICAL AND CHEMICAL CHANGES

Sedimentation of red cells

Correction of the sedimentation rate for anaemia

- 167 When the sedimentation rate is determined by Wintrobe's method (see Vol II, p 493) the tube may afterwards be centrifugalized to determine the corpuscular volume.

Fragility of the red cells

Quantitative method

Fragility is influenced by a number of physical factors which, for an accurate test, must be eliminated as far as possible. The carbon dioxide content of the blood has a definite effect, and this may be avoided by fully oxygenating the blood under test. Other sources of error are inaccurate saline solutions, failure to mix properly, and variations in the pH of the distilled water used for diluting the saline. This last is minimized by using whole blood at a dilution of 1 in 25 which allows the blood plasma to act as a buffer (Creed). Distilled water should be boiled and stored in bottles with a soda-lime air filter in order to prevent absorption of carbon dioxide. Anaemia *per se* decreases fragility, an anaemic person may therefore not exhibit minor degrees of fragility until the anaemia is cured (Creed).

Method based on Creed's technique

A stock 25 per cent solution of sodium chloride in distilled water is prepared from the pure salt which has been dried to constant weight by heating and allowing to cool in a desiccator. At the time of the test, 4 cubic centimetres of this stock solution is diluted with distilled water in a measuring cylinder to 100 cubic centimetres to make a 1 per cent solution and is mixed thoroughly. The distilled water must be reliable. A series of 12 tubes ($3\frac{1}{2} \times \frac{3}{8}$ inch) are set up in a rack. To the various tubes, using a teated dropping pipette, are added the number of drops of distilled water and of 1 per cent sodium chloride solution according to the following table. This gives a series of saline concentrations ranging from 0.28 per cent to 0.72 per cent with intervals of 0.04 per cent. It is essential to ensure thorough mixing of the saline and distilled water before proceeding to the next step, namely, the addition of one drop of blood to each tube in the series.

Distilled water																	
(drops)	-																
1 per cent NaCl	-	18	17	16	15	14	13	12	11	10	9	8	7				
(drops)	-																
Concentration NaCl	-	7	8	9	10	11	12	13	14	15	16	17	18				
(per cent)	-	0.28	0.32	0.36	0.40	0.44	0.48	0.52	0.56	0.60	0.64	0.68	0.72				

As to the blood used for the test, Creed collects this from a vein with a dry sterile needle, allowing the blood to run directly into a wide test-tube which has previously been waxed to prevent clotting. Others use heparinized blood, or blood that has been collected into Wintrobe's isotonic ammonium and potassium oxalate mixture (see p. 46). The blood must be thoroughly oxygenated, either by blowing a current of air vigorously over the surface by means of a hand bellows with a glass delivery tube drawn out to a wide capillary, or by rolling the blood around in a wide bottle or a large tube. Aeration should be carried out for 4 minutes. After adding the blood, the tubes are inverted to ensure mixing, and this is repeated 10 minutes later. After a further 10 minutes the tubes are centrifugalized, and the degree of haemolysis is assessed by comparing the amount of haemoglobin in the supernatant fluid matched against a series of standards made from the actual blood used for the test. These standards are prepared as follows: To 100 drops of distilled water are added 4 drops of blood. Of this haemoglobin solution, 20, 16, 8, 4, 2, and 1 drop are placed in a series of tubes and the volume of each is made up to 25 drops. The series then contains an amount of haemoglobin equivalent to 80, 64, 32, 16, 8, and 4 per cent of haemoglobin in the actual test. The supernatant fluid in the test proper can be compared with these standards against a piece of white paper. The following are the observed limits of normal variation, using Creed's technique:

NaCl per cent	—	—	0.28	0.32	0.36	0.40	0.44
Haemolysis per cent	—	—	98-100	90-98	45-90	10-46	0-10

Bilirubinaemia

Determination of plasma bilirubin

The principle of this method is colorimetric comparison of the red colour produced by bilirubin in the presence of diazotized sulphanilic acid with an artificial standard containing methyl red.

Standard reagents Solution A 1 gramme of sulphanilic acid is dissolved in 250 cubic centimetres of N hydrochloric acid and diluted to 1 litre with water Solution B 0.5 gramme of sodium nitrite in 100 cubic centimetres aqueous solution The reagent is freshly prepared, as required, by mixing 0.3 cubic centimetre of solution B with 10 cubic centimetres of solution A

Standard—Stock methyl red solution 0.29 gramme of pure methyl red is dissolved in glacial acetic acid and diluted with the same acid to 100 cubic centimetres. Standard methyl red solution 1 cubic centimetre of the above stock solution, 5 cubic centimetres of glacial acetic acid and 14.4 grammes of crystallized sodium acetate are made up to 1 litre with water. This solution, at pH 4.63, contains 2.9 milligrams of methyl red per litre, and matches the colour obtained when 0.1 milligram of bilirubin is treated with diazo reagent in a final volume of 25 cubic centimetres.

Method—Quantitative reaction 1 cubic centimetre of plasma or serum is treated in a centrifuge tube with 0.5 cubic centimetre of diazo reagent, 0.5 cubic centimetre of saturated ammonium sulphate, and finally 3 cubic centimetres of absolute alcohol. The mixture is stoppered, thoroughly shaken, and filtered after a few minutes. The colour of the filtrate is matched against the standard in the colorimeter, using a green-light filter. The reading of the standard divided by the reading of the unknown and multiplied by 1.6 gives the milligram of bilirubin per 100 cubic centimetres of plasma or serum. 1 milligram of bilirubin equals 2 units.

Direct reaction—If the diazo reagent is carefully 'layered' above the plasma and the tube allowed to stand for a few moments, a positive 'direct' reaction is shown by a red colour at the liquid junction.

The normal level of plasma bilirubin obtained by this method varies from 0.2 to 1.7 milligram per 100 cubic centimetres, although most normal results are below 0.8 milligram per 100 cubic centimetres.

MISCELLANEOUS

Haemoglobin derivatives

Methaemalbumin (pseudo-methaemoglobin)

This pigment is found in blackwater fever and other haemolytic anaemias (Farley and Bromfield^{1,2}, it is similar in structure to methaemoglobin except that the pigment is combined with plasma albumin instead of globulin, it is extracorpuscular and cannot act as a respiratory pigment. Only the serum albumin of human beings and monkeys can form this substance. The spectrum closely resembles that of methaemoglobin, but careful examination has shown that the α band is at 6240, instead of at 6300, as in the case of methaemoglobin (See also p. 42).

CUMULATIVE SUPPLEMENT 1945

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BLOOD PRESSURE, HIGH AND LOW HIGH BLOOD PRESSURE

Essential hypertension

Aetiology

170

The work of Goldblatt which has been going on since 1934 has elucidated many of the problems of hypertension. Experimental constriction of the renal arteries is used to produce ischaemia of the kidney, and hypertension is the result. The renal factor has become prominent once more. It can now be said that hypertension is due to the constriction of the arterioles at the periphery, and that the factor causing this is a chemical agent and not alteration in nervous mechanism. Further experiments in artificial renal hypertension prove that if the renal artery is constricted sufficiently to lead to excessive tension in the renal tissue the enzyme, renin, combines in the blood with a substance, pre-angiotonin (pre-hypertensin), which probably comes from the liver, so that a new pressor substance called angiotonin or hypertensin is formed. In addition there is a fourth factor, hypertensinase, which destroys angiotonin *in vitro*. Renin has been shown to exist only in the renal cortex and then in an extremely unstable form. It is quite probable that the afferent arteriolar narrowing in the kidney is sufficiently widespread to set free renin in amounts requisite to raise the arterial pressure. The kidney circulation is controlled by the renin hypertensin system through the medium of the nephrones.

Pickering points out that two kinds of structural change have been observed to occur in the small vessels. First, the tunica intima becomes thickened by fatty and hyaline deposits, chiefly in the renal arterioles and again more especially in the afferent glomerular vessels, this condition is found in about 98 per cent of patients with essential hypertension, the other organs appear to be less commonly affected. The second change is represented by a condition of necrosing arteriolitis, so called by Fahr, here in the tunica media or tunica intima there are found collections of granular matter—this is invariably present in the kidney tissues and sometimes in other organs when the malignant type of hypertension exists, but it is never seen in the benign type. It is clear, however, that these lesions are the effect and not the cause of essential hypertension because they respond normally to the usual tests for dilator and depressor effect. Pickering considers that spasm is the main aetiological factor and from his experiments believes that such spasm is of humoral and not of nervous origin. Furthermore he thinks that it affects mainly the efferent glomerular arterioles of the kidney and the skin and cerebral vessels slightly, the arterioles of the voluntary muscles, however, are hardly influenced by such spasm.

Coming to the subject of acute nephritis Pickering believes that the hypertension here is likely to be nervous in origin. The chemical substance, if it is in effect active, is uncertain in nature, it is not adrenaline but probably renin. It may be that renin is released from the kidney when the intraglomerular pressure is lowered, so far no proof of this has been forthcoming.

It is clear according to Smith, Goldring and Chasis that unilateral renal disease does not predispose to hypertension, these workers state that in the recorded literature there are only 11 cases in favour of the argument for unilateral renal disease, and it may therefore be concluded that this is rarely a cause of hypertension in man. The theory of primary renal origin still being unproved physiologically, pathologically or surgically, the original of essential hypertension must still be regarded as unknown, in the words of these writers the kidney appears to be the victim rather than the culprit.

HIGH BLOOD PRESSURE IN GENERAL

Treatment

General treatment

Evans and Loughnan analysed the effects of 33 drugs or preparations, including nitrates, iodides, sedatives, xanthine and choline derivatives, vegetable extracts, and hormones, on the blood pressure and symptoms of 70 persons with hyperpiesia (essential hypertension). After elimination of possible fallacies and comparison with control cases given placebos, it appeared that none of the 33

BLOOD PRESSURE—BLOOD TRANSFUSION

preparations had a hypotensive effect on the patients with essential hypertension. Symptomatic improvement, more than that due to placebos, followed the use of 6 preparations only, namely bismuth subnitrate, iodine and iodides, bromides, phenobarbitone sodium, theominal (theobromine and phenobarbitone), and potassium thiocyanate.

Various groups of cases have been collected, the patients in which have been treated surgically by sympathectomy. Each series is small in numbers, but the period of observation is generally from 3 to 7 years after the operation, the supradiaphragmatic or the infradiaphragmatic route may be chosen. Bordley, Galdston and Dandy report on 10 patients, 9 were relieved of their symptoms after the operation and in 5 the arterial pressure was lowered. Of these 5, however, 4 showed a rise of blood pressure later and all the symptoms returned to pre-operative levels.

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BLOOD TRANSFUSION

GENERAL EFFECTS OF STORED BLOOD

Therapeutic effects of stored blood

All reports go to show that stored blood is entirely effective in temporarily replacing lost blood and in this respect the benefit to be expected from any particular quantity is similar to that from fresh blood. It appears that the life of recently stored erythrocytes in the circulation is almost if not quite as long as that of fresh cells. Haemoglobinuria is not noticeably commoner after stored blood transfusion if the blood is not too old. In stored cells the potassium falls and the sodium rises but, if not stored too long, the cells rapidly become reconditioned after transfusion. Evidence has steadily accumulated that fresh or relatively fresh blood is preferable to stored blood for stimulation of haemopoiesis and for antibacterial powers. For acute infections, acute haemolytic anaemias, the purpuric states or any conditions requiring haemoplastic elements, fresh whole blood is certainly best.

DETERMINATION OF BLOOD GROUPS

The 'ABO' or international system of nomenclature has been adopted by the Emergency Medical Service and the British Red Cross donor service and is now used almost exclusively in Great Britain.

Thus the 'universal donor' is now Group O and the 'universal recipient' Group AB. It is important to remember that the above letters indicate the presence in the cells of one, both, or neither of the 2 agglutinogens A and B. In view of the popularity of plasma transfusions, the agglutinin content of the corresponding plasmas should also be recalled. They are, as indicated by the Greek letters,

MOSS GROUP	INTERNATIONAL GROUP	RED CELL AGGLUTINOGENS	PLASMA AGGLUTININS
4	O	O	$\alpha\beta$
2	A	A	β
3	B	B	α
1	AB	AB	—

Thus for transfusion, the ideal plasma is that of Group AB because it contains no agglutinins and cannot, therefore, affect the recipient's cells. But this is a very rare group and most of the plasma available belongs to Groups O and A. Given in quantities up to 500 cubic centimetres these plasmas are known to have no ill effects, a certain degree of agglutination among the recipient's cells being harmless. But when large quantities are given, or if the patient is very anaemic, it is well to make sure that the α and β titres of the plasma are not, as they are in a few bloods, exceptionally high (Knott and Koerner). To guard against this it is well to cross-match some of the plasma diluted 1 in 25 with an equal volume of a citrate suspension of the patient's cells. Should these agglutinate it is advisable not to give large volumes of the particular plasma or, if large volumes must be given, one of lower titre should be used.

A further point brought out when testing blood groups is the need for standard grouping serums of really high titre (Taylor, Race, Prior and Iken¹), otherwise a certain number of AB bloods may be wrongly diagnosed as A. In some AB cases the factor B is partially dominant to, and may easily obscure, the A factor until tests are made with really powerful anti-A serum, that is one reacting in dilutions as high as 1 in 100. From the Galton Laboratory more recently has come also further valuable suggestions for the more accurate determination of groups and performance of cross-matching tests. Essentially the new technique (Taylor, Race, Prior and

Iken²) consists of testing not only the cells against anti-A and anti-B serums, but also the serum against A and B cells, the tests being made in test-tubes and not on slides. The same tube technique should be adopted for cross-matching also. This paper by Taylor, Race, Prior and Iken should be read by all practitioners who are directly concerned with blood transfusion.

Emphasis has been laid upon the importance of the sub-groups A1 and A2 and also upon the recently discovered Rh factor, the existence of all of which are concerned with the reactions that are sometimes seen in second and later transfusions in the same patient, or in the transfusions given to obstetrical patients. This matter and also the new grouping technique are dealt with at length in an admirable Harveian Lecture by Whitby, who discusses the whole question of reactions and hazards.

TECHNIQUE OF TRANSFUSION

Blood transfusion in war-time

The impossibility of obtaining at very short notice in war-time a sufficient supply of living donors, either in the field or in towns under aerial bombardment, has resulted in much work upon the use of stored blood and the institution of 'blood banks'. In the London and Home Counties areas a series of depots has arisen under the Emergency Medical Service, the Army has developed its own organization for storing and despatching blood to places at some distance, in most provincial areas similar schemes have been developed. The source of blood has been large panels of volunteer donors. Both Group O and Group A bloods have been stored, since, when there is time to group the patients, the latter will be found suitable for at least 40 per cent of them. The bloods have been collected in sterile screw-capped bottles containing anticoagulant solution and stored in the cold room or a smaller refrigerator at temperatures of 2° to 4° C. It took a short time to discover the most satisfactory anticoagulant for stored blood but agreement seems now to have been reached that 100 cubic centimetres of 2.5 per cent sodium citrate, 20 cubic centimetres of 15 per cent glucose and 420 cubic centimetres of blood make the best mixture for storage (Maizels and Whittaker^{1, 2}, Aylward, Mainwaring and Wilkinson). Chemical changes in the blood during storage seem to be reduced to the minimum when a truly isotonic solution of this type is used, and the most recent reports (DeGowin and Hardin; Brewer, Maizels, Oliver and Vaughan) suggest that reactions are not to be expected after transfusions even when storage has continued for 3 weeks or a little more. However, it is still inadvisable to use blood more than 4 weeks old. The blood must not freeze, because it becomes toxic when thawed. It must be kept in the dark and not be agitated, otherwise early haemolysis occurs, in any case under the most favourable conditions, haemolysis commences within a week. But slight haemolysis gradually rising into the amber supernatant plasma is not a contra-indication to use. Gross relatively rapid haemolysis, tinging the whole plasma red and indicating infection during collection, should result in discarding of the blood. In order to avoid minor incompatibility, the principle of mixing at least 6 bloods of the same group was adopted during the Spanish civil war and in this way, by using only universal donors, preliminary grouping was altogether avoided. But if the stored blood is not of the mixed universal donor type, then the usual preliminary grouping and cross-matching must be done. At the time of collection each bottle of blood should be accompanied by 2 smaller samples from the patient, one (clotted) for a Wassermann reaction and one (citrated) for grouping. From the storage bottle the blood may be transfused by any of the methods usually employed for fresh blood or, if great speed is necessary, a positive pressure may be created inside the storage bottle and allowed to drive the blood directly through a tube and a needle into the patient's vein. If the blood is to be used fresh or is not to be stored for more than 2 days, glucose may be omitted and 9 parts of blood may be collected simply into one part of sterile 3.8 per cent sodium citrate solution. For rapid work numerous devices are now being tried.

Apparatus and procedure

Transfusion of stored plasma and serum

As already mentioned, plasmas from Groups O and A have already been extensively used in resuscitation work, particularly in treatment of shock such as occurs with severe burns. The plasma is aseptically pipetted off from blood collected in the storage bottles already described and after rebottling may be kept almost indefinitely at cool room temperatures. Plasma does not have to be stored in the cold room. Some samples tend to deposit fibrin on standing so that, before transfusion, filtration may be advisable. In the early days plasma filtration caused much trouble but considerable improvements have now been made (Macfarlane, MacSween, Mainwaring and Parish). The methods of plasma transfusion are exactly similar to those used for whole blood and the quantities which may be given are similar. One or two necessary precautions have already been mentioned. Both serum and plasma may, for storage purposes, be dried to a powder at low tempera-

ture *in vacuo*, and when redissolved in sterile distilled water form reconstituted material which is therapeutically just as effective as the fresh (Edwards, Kay and Davie) This has made it possible to distribute plasma very widely in dried form, with corresponding improvement in resuscitation work under field and other difficult conditions These dried preparations are absolutely permanent and, if there were sufficient drying plants in the country, would probably supersede the wet stored products Several small-scale rapid drying methods have been suggested, and shortly a generally available method is certain to be devised The requirements were fully reviewed in a leading article in the *Lancet* As already explained, the ideal product is one derived from Group AB blood, because it is devoid of agglutinins and cannot therefore affect the patient's cells As this is a very rare group, it is important to note that a similar plasma can be obtained artificially by mixing equal volumes of fresh Group A and Group B bloods and storing this mixture for a few days in the cold room During that time the respective agglutinins β and α act upon the cells, are absorbed, and when the remaining plasma is drawn off it is agglutinin-free, that is equivalent to that of Group AB Stored plasma as well as stored blood is now being issued by the E M S depots There is some evidence (Brennan) that it can be effective as a haemopoietic stimulus after blood loss, in which case a much wider field than the treatment of shock alone becomes open to plasma transfusion Serum is found to be therapeutically as effective as plasma and is easier to handle Repeated filtration is not required, because little or no precipitation occurs during storage The yield per volume of blood collected from the donor is not quite so good as in the case of plasma It has been said that serum is more toxic than plasma but experience in Great Britain has not confirmed this as yet

Concentrated erythrocytes

There is now also a method of giving large numbers of cells without a correspondingly large volume of fluid This is the 'packed cell' technique Citrated blood is left for a few days to settle, the plasma is then pipetted off and only the residual 'packed cells' are used for transfusion They give great oxygen-carrying capacity in any small volume, and in any of the above circumstances in which either rapid improvement of the cell count is required or there is cardiac weakness, the giving of concentrated cells should be considered

Continuous drip transfusion

Practically all the recognized methods of performing intravenous drip transfusions of saline, glucose and saline, or gum saline may be adapted for the administration of citrated blood To avoid rigors, which at once interrupt administration and therefore negate all the advantages of the continuous method (Knott and Leibel), particular care must be taken that all the apparatus is chemically as well as bacteriologically clean The settling of erythrocytes into a compact layer tending to block tubes and needles must be avoided either by gently rotating the reservoir at intervals or, better still, by slowly bubbling oxygen through the blood Provision must be made to filter off any small clots which have formed during collection of blood from the donor Also a few special points arise concerning the donors used for continuous transfusion The bloods from the different donors must be perfectly compatible not only with that of the patient but also with each other This implies that they must all be of the same group and must cross-match perfectly For single transfusions, when the patient belongs to a group other than Group O, the donor may be 'universal' or belong to the patient's own group But for continuous transfusion the donors must all be 'universal' or all of the same group as the patient the reservoir must never contain a mixture of groups When really large volumes of citrated blood are to be given, the donors should always be of the same group as the patient Unless the patient is of group O, universal donors should not be used for continuous drip transfusions, for this reason It will be seen from the table above that the plasma of universal donors contains the agglutinins α and β and it has been shown (Knott and Koerner) that such plasma will sometimes agglutinate the cells of any other group in very high dilutions Transfusion of large volumes of such high titre plasma may agglutinate so many of the patient's own cells that reactions and haemoglobinuria soon occur Such universal plasma given as single 1-pint transfusions practically never causes trouble But the situation is very different when much larger volumes are given continuously

Viscose tubing

In blood transfusion 10 per cent of the patients have reactions, despite all the precautions taken with regard to blood grouping and solutions used According to Naftulin, Wolf and Levinson there are 3 sources for these reactions (1) the distilled water used—it may contain pyrogenic substances, (2) the chemicals used in the solutions—impurities may be present, (3) equipment—the latter may not be suitable or it may be imperfectly cleansed after each transfusion It is believed that rubber tubing especially has intrinsic defects A new rubber tube contains sulphur and other substances which have to be got rid of before it can be said to be pyrogen free and

it is also very difficult to say with certainty that all protein is eliminated even after the most meticulous washing. In the Michael Reese Hospital, Chicago, infusions of whole blood, plasma or serum are given through viscose tubing which is very thick and which has been specially prepared, it is discarded after use as it is not expensive in price. In a record of 1,137 blood transfusions given through viscose tubing there were pyrogenic reactions in only 0.64 per cent.

REACTIONS AFTER TRANSFUSION

The matter has been so completely dealt with by Whitby in his Harveian Lecture that reference to this should be made. The important point is that the large majority of reactions are avoidable.

Transfusion accidents

Rhesus factor

Levine reports observations on intra-group transfusion accidents associated with pregnancy, which reveal the importance of the concept of isoimmunization of the mother by hereditary dominant blood factors in the foetus transmitted from the father. The blood factor generally involved is similar to, or is identical with the Rh antigen described by Landsteiner and Wiener. Tests in pregnant women suffering from transfusion accidents show that about 85 per cent of all the human blood samples tested contain the Rh factor, that is they are Rh positive, and the remaining 15 per cent are Rh negative. These studies throw some light on the pathogenesis of the familial haemolytic disease, erythroblastosis foetalis, and suggest a modified compatibility test for the prevention of intra-group transfusion accidents after repeated transfusions, or in pregnancy at the first transfusion. Recent investigations indicate that the Rh factor is responsible in the majority of such cases. For safer transfusion it is suggested that a list of Rh negative donors in all groups, or at least in Groups O and A, should be available.

Aylward, F. X., Mainwaring, B. R. S., and Wilkinson, J. F. (1940) *Lancet*, 1, 685.

Brennan, H. J. (1940) *Brit med J*, 1, 1047.

Brewer, H. F., Maizels, M., Oliver, J. O., and Vaughan, Janet M. (1940) *Brit med J*, 1, 828.

DeGowin, E. L., and Hardin, R. C. (1940) *Brit med J*, 2, 1.

Edwards, F. R., Kay, J., and Davie, T. B. (1940) *Brit med J*, 1, 377.

Knott, F. A., and Koerner, E. H. (1939) *Lancet*, 2, 1069.

— and Leibel, B. (1941) *Lancet*, 1, 409.

Landsteiner, K., and Wiener, A. S. (1940) *Proc Soc exp Biol, N Y*, 43, 223.

Leading Article (1941) *Lancet*, 2, 104.

Levine, P. (1941) *Amer J clin Path*, 12, 898.

Macfarlane, R. G., MacSween, J. C., Mainwaring, B. R. S., and Parish, H. J. (1942) *Brit med J*, 1, 377.

Maizels, M., and Whittaker, N. (1939)¹ *Lancet*, 2, 1219.

— (1940) *ibid*, 1, 113, 590.

Naftulin, H., Wolf, A. M., and Levinson, S. O. (1943) *J Amer med Ass*, 123, 321.

Taylor, G. L., Race, R. R., Prior, A. M., and Iken, E. W. (1940)¹ *Brit med J*, 1, 297.

— — — (1942)² *J Path Bact*, 54, 81.

Whitby, L. E. H. (1942) *Lancet*, 1, 581.

BONE DISEASES

TUMOURS OF BONE

Non-malignant

Melorheostosis

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This is a rare bone disease and a case recently recorded showed that the right leg had been longer than the left since the patient was the age of 10 years. At the time of examination she was 41 and a spinster and had had a plantar fasciotomy for acquired pes cavus. There was a history of 10 or 15 years regarding ulceration on the dorsum of the right foot. There was permanent increase in the growth of the right leg. At the right side of the skull and raised about one inch above the normal part there was a large bony mass springing from the right parietal and temporal bones. In addition to this the right half of the mandibular body was enlarged. On X-ray examination typical melorheostosis conditions were found in many of the bones on the right side of the body. In the soft tissues the changes consist of tense nodular deposits, in the case under review these were to be found at the medial aspect of the lower end of the right femur and at the right ankle. The condition arises from a hyperostosis of the bony cortex and the lesion is said to resemble molten wax streaming down one side of a candle. Franklin and Matheson in describing the particular case under their care said that the excess of bony tissue appears to be poured down one side of the bone, hence the name melorheostosis.

Malignant*Ewing's sarcoma*

Certain observers consider that Ewing's tumour is not endothelial in origin and they choose to classify it as a reticulosarcoma, thus coming into line with Oberling. Swenson made investigations on 26 cases, chiefly with regard to the radiological factors, and examined records and pathological specimens, there being 42 items in his report, he states that the cells are structureless in most cases but they resemble immature erythrocytes, reticulum cells and capillary endothelial tubes. 3 patients in every 5 are males. Metastases are found in lungs, bones or brain. So far as the radiographical examination is concerned there is very little to be seen, a biopsy is therefore more satisfactory. The tumour although it is not osteogenic itself nevertheless stimulates increasing bone formation. Of the 26 cases investigated by Stout only 4 showed the classical 'onion skin' pattern described originally by Ewing. In treatment by X-ray the whole bone was dealt with by cross-fire technique, with a maximum dose of 4,500 r. As proof of the great malignancy of Ewing's sarcoma, about 80 per cent of patients succumb after an average survival period of 15 months.

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Franklin, Emily L, and Matheson, I (1942) *Brit J Radiol*, **15**, 185

Stout, A P (1943) *Amer J Roentgenol*, **50**, 334

Swenson, P C (1943) *Amer J Roentgenol*, **50**, 343

BRAIN ABSCESS**AETIOLOGY**

In the examination of pus from brain abscesses anaerobic culture is essential, this allows for the isolation of obligate anaerobes and of certain strains of pneumococci. A single organism is found in about 68 per cent of cases and the organisms are multiple in 29 per cent, 3 per cent of the specimens are sterile. The chief organisms concerned are *Staphylococcus aureus*, fusiform bacilli, anaerobic streptococci, *Streptococcus pneumoniae*, *Proteus vulgaris* and *Streptococcus pyogenes*. A general conclusion cannot be drawn about the rate at which the abscess capsule is formed or the relation of the rate of formation to the type of infecting organism (McFarlan).

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McFarlan, A M (1943) *Brit med J*, **2**, 643

BRAIN REGIONAL DIAGNOSIS**DISORDERS OF FUNCTION PRODUCED BY DISEASE OR INJURY****Electroencephalogram investigations***Deviations from the normal*

Adrian summarizes the present state of knowledge, the uses, significance and limitations of the electroencephalogram, which is an important aid to research on the brain, normal and abnormal. It is a record of the electrical activity of the cerebral cortex, made by placing electrodes on the scalp, amplifying the potential changes, and recording them with some form of oscillograph. The subject when examined may be sitting up or lying down, awake or asleep, for all the time his brain normally gives rise to a succession of potential. The nerve cells of the cortex constantly vary in activity. In 1928, Berger, Director of the Psychiatric Institute at Jena, published records made with the string galvanometer from the heads of a number of subjects, showing a regular potential oscillation at a frequency very close to 10 a second. The waves (Berger's X rhythm) appear when the subject closes his eyes and disappear when he opens them and when he is startled, and are usually larger and more regular over the occipital region, although they are also present over the frontal region. Electroencephalograms may be abnormal in 3 directions: (1) completely absent, as in cases in which a blood clot or cyst separates the cortex from the skull, and when a tumour occupies part of the cortex, this is of value in localization of a lesion, (2) diminished electrical activity, as shown by irregular slow fluctuations of potential, this may be localized, as near an infiltrating tumour of the cortex, or widespread when the brain is bruised or lacerated, it also occurs in sleep, coma and anaesthesia due to various drugs, (3) excessive electrical activity, as in an epileptic fit. In these 3 forms records made from different points on the scalp will show whether the abnormality is localized or general. In mental diseases there is rarely any deviation from the normal.

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Significance of abnormal electroencephalograms

The significance of an abnormal electroencephalogram is investigated by Williams, 900 subjects, divided into groups of selected normal persons, normals, psychoneurotics, epileptics and persons with post-traumatic symptoms, were examined. The author suggests that a non-specific diagnosis of epilepsy should be made from the abnormalities observed in the electroencephalograms, but that a diagnosis of the specific type must be based on the clinical signs. It is concluded that an abnormal electroencephalogram in otherwise normal persons is strong evidence of an inborn abnormality involving the central nervous system, it may be manifested in a patient or in his offspring as a behaviour symptom—psycho-neurotic, psychopathic, psychotic or epileptic in type. About 40 per cent of epileptic

- 188 patients have a normal electroencephalogram during the period between their fits
In diagnosis and prognosis

The diagnostic and prognostic value of the electroencephalogram was examined by Gibbs, who states that the electroencephalogram is of value for both diagnosis and prognosis in cases of epilepsy, brain trauma, encephalitis and behaviour disorders, it is of use for diagnosis only in narcolepsy and in Schilder's disease, for diagnosis and localization in epilepsy, brain tumour, traumatic lesions, abscess and subdural haematoma and for prognosis only in meningitis and Sydenham's chorea

Adrian, E D (1941) *Camb Univ med Soc Mag*, 18, 57

Gibbs, F A (1942) *J Amer med Ass*, 118, 216

Williams, D (1941) *J Neurol Psychiat*, 4, 257

BRAIN TUMOUR

DIFFERENTIAL DIAGNOSIS

General review

- 189 In the diagnosis of brain tumour the main questions to be answered are 2 in number the first refers to the presence or absence of a brain tumour or some other form of intracranial lesion like a tumour, the second is concerned with the site and pathology of the tumour when it is known to be established With present-day means at his disposal the neurological surgeon can affirm that a tumour is present, always provided that he has the facility for carrying out a complete investigation Again it has to be remembered that there is the text-book type of cerebral tumour with all its classical signs and a second group which may satisfy the neurological investigation but which may be lacking in classical symptoms Lumbar puncture should seldom be employed as it is a dangerous procedure in these cases Horrax has reviewed and classified the cerebral tumours into 2 groups as follows (1) those which are not always benign—meningiomas, acoustic neuromas, cholesteatomas, slow-growing gliomas, pituitary adenomas and pinealomas, (2) tumours which are 'silent', giving very little neurological evidence of their position and which may take the form of gliomas and third ventricle tumours The outlook in the case is completely dependent upon the successful removal of the brain tumour and upon the possibility of leaving the adjacent structures undamaged The radiological treatment of malignant brain tumours is very disappointing The situation may be summed up by saying that about 50 per cent of all brain tumours may be removed satisfactorily and completely and the survivors of such an operation in 75 per cent of cases go back to work

Horrax, G (1943) *Bull N Y Acad Med*, 19, 125

BRAIN: VASCULAR DISORDERS

CEREBRAL ANEURYSMS

Clinical picture

- 190 The only condition found often enough to be of causal significance was arterial hypertension in 16 cases, or 13 per cent, of these, 10, or 62 per cent, proved fatal, thus suggesting a bad prognosis, for 50 per cent of patients recover from a first attack, this percentage is a much better recovery rate than that of primary cerebral haemorrhage Migraine was reported in 4 cases Although acute mycotic and arteriosclerotic aneurysms may occur on the cerebral vessels, the great majority of the intracranial aneurysms are the saccular, 'congenital', 'developmental', 'bifurcation', or berry form which occurs in the angle formed by the bifurcation or branching of the arteries of the circulus arteriosus of Willis Histological examination of the walls of the berry aneurysms confirmed the fibrosis and defect in the middle coat and showed changes in the elastic tissue, the arteries may be normal elsewhere The defects of the middle coat may occur without the formation of berry aneurysms The aneurysms are rare in infancy and seldom seen before adolescence The age of onset ranges from 21 to 84 years, with an average of 50 years Among 40 cases there were 18 males and 22 females The aneurysm is usually single, in the authors' series this was so in 30, in 7 cases there were 2 aneurysms, and in 3 cases 3, in all 51 berry aneurysms The most frequent sites for berry aneurysms were the middle cerebral artery in the fissura cerebri lateralis of Sylvius (16), the angles between the anterior cerebral and anterior communicating arteries (13), and the bifurcation of the internal carotid (11) It is well known that syphilis, which is responsible for 90 per cent of aneurysms elsewhere in the body, plays little or no part in cerebral aneurysms The miliary aneurysms described by Charcot and Bouchard in ordinary cerebral haemorrhage are now regarded as really false dissecting aneurysms of very arteriosclerotic vessels The onset occurs suddenly in about 90 per cent, and 70 per cent of the patients are 50 years of age or more Strenuous effort does not seem to exert much influence in precipitating the onset In 27 cases of ruptured aneurysm, subarachnoid haemorrhage of varying degree occurred in all, and in 8 was confined to that region, in 19 cases intracerebral and subarachnoid haemorrhages were both found The intracerebral haemorrhages occurred primarily in 2 positions, frontal and temporal Headache is the first symptom in most cases, loss of consciousness

comes next, and its early onset makes the prognosis a little worse than in cases without loss of consciousness. With advancing years the prognosis becomes worse, the average age of the fatal cases was 10 years higher than that of the survivors, the oldest survivor was 72.

Berry aneurysms

Richardson and Hyland present clinical and pathological observations on sub-arachnoid and intracranial haemorrhage caused by the rupture of berry aneurysms. This generously illustrated and elaborate paper is based on material obtained at the Toronto General Hospital during the years 1928–38 inclusive: namely 118 cases of spontaneous subarachnoid haemorrhage, 8 cases of large unruptured aneurysms producing pressure symptoms, and 9 cases in which at necropsy there were found to be unruptured berry aneurysms without known symptoms. The authors regard spontaneous subarachnoid haemorrhage as practically always (90 per cent) due to rupture of a berry aneurysm. Of the 118 cases 61 proved fatal, and in November, 1938 it was found that of the 57 original survivors, 37 were alive from 1 to 10 years after the attack.

Treatment

The most important factor is complete rest in bed for not less than 6 or 8 weeks. There has not been any essential difference in the outcome of cases treated with or without repeated spinal drainage, lumbar puncture should be performed only for diagnosis, and then as indicated for relief of symptoms.

Richardson, J. C., and Hyland, H. H. (1941) *Medicine, Baltimore*, 20, 1.

BREAST DISEASES

TUMOURS AND THEIR TREATMENT

Malignant tumours

Carcinoma

Summary of main factors—The review of 640 cases of cancer of the breast provides ample data from which main conclusions may be drawn. In several cases radical mastectomy was performed. Twenty patients died as a result of the operation and for various reasons others could not be kept under subsequent observation. Nevertheless 599 were observed continuously for 5 years. The number of patients who died in the 5-year period amounted to 290 who died on recurrence, 12 who succumbed to intercurrent disease without any associated recurrence and 13 whose death was certified as being from 'unknown causes'. Of the remainder, 33 were alive although recurrence had taken place but 231 were alive without recurrence 5 years after the operation. The percentage of survivals in this series (Haagensen and Stout) was therefore just over 36 per cent. Furthermore it is generally agreed that the earlier the operation the better the chance of survival, especially when there is subsequent irradiation treatment. This is proved by reference to the series of 1,879 cases reported by McWhirter, who showed that the survival rate was emphatically increased when surgery was amplified by radiotherapy. As a general rule it may be said that if a patient remains free from recurrence she is likely to survive for at least 5 years.

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Haagensen, C. D., and Stout, A. P. (1942) *Ann. Surg.*, 116, 801.
McWhirter, R. (1943) *Edinb. med. J.*, 50, 193.

BRONCHIECTASIS, BRONCHIOLECTASIS, AND BRONCHIAL SPIROCHAETOSIS

BRONCHIECTASIS

Aetiology

Results of bronchography

Since the introduction of bronchography, by which it is possible to obtain a fairly accurate picture of the bronchial tree as a whole, the notion of bronchiectasis as an anatomical state rather than as a clinical entity has gradually gained in favour. This has modified in no small degree the traditional teaching in regard to this disease, which was based largely on statistics drawn almost entirely from records of advanced cases in which the effects of infection were seen at their maximum. Such records took little or no account of the lesser degrees of bronchiectasis or of the occurrence of relatively uninfected cases which, in days when radiography was yet in an embryonic state, gave practically no clinical evidence of the existence of any material structural changes in the respiratory tract (Davidson).

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Sinusitis and bronchitis

Paranasal sinusitis, acute and chronic, has been found to be associated with bronchiectasis in over 5 per cent of cases. Furthermore, with regard to the latter category, in one-half of the number of cases sinusitis and bronchiectasis began simultaneously. In a series of 405 cases reported by Simonton there were 23 instances

of bronchiectasis and in no case did bronchiectasis precede sinusitis. It seems that bronchiectasis and sinusitis occurring in such close association are caused by an acute respiratory infection of severe type. Mutual reinfection is made very easy by carriage of the infective material along the air passages.

Treatment

Combined sinusitis and bronchiectasis

The results of treatment in 65 cases of combined chronic sinusitis and bronchiectasis prove that radical treatment of both conditions is essential. When the sinuses are operated on only, the results indicate only partial success. On the other hand when the sinus operation is performed and a complementary lobectomy is done, the chest symptoms show pronounced or moderate improvement in 90 per cent of cases, the sinus symptoms may disappear altogether and they are alleviated in at least 70 per cent of cases. If lobectomy alone is done and the sinuses left, whereas the chest symptoms show improvement in about 85 per cent of cases the sinus symptoms are very little affected in 75 per cent of cases (Goodale).

In all these cases the cooperation of the rhinologist, bronchoscopist, physician and surgeon is essential.

Simonton states that it is better to defer radical treatment of the sinusitis until the bronchiectasis has been dealt with.

Surgical treatment of primary non-tuberculous bronchiectasis

The success of surgical treatment for bronchiectasis is reflected in the mortality rate. Generally speaking, in untreated cases 35 per cent of the patients die, but this figure is reduced to about 15 per cent when operative measures are adopted. When treatment by lobectomy is carried out infection is always the danger after operation and various measures for dealing with this menace—pre-operative preparation, postural drainage and so on—are indicated. Bradshaw and O'Neill emphasize that sulphonamides do not have any effect when administered before operation and they also advise that lobectomy should not be performed until at least 6 weeks have elapsed after bronchography has been done. A simple routine adopted in most cases is premedication with nembutal and induction of anaesthesia with cyclopropane, during the operation endotracheal ether and oxygen are used. The statistics of lobectomy are as follows. In 24 patients with lower lobe or lower lobe and lingula disease removal of all diseased tissue was possible, the mortality was 4.2 per cent. Of 26 patients who had one lobe removed, with active disease allowed to remain in other lobes, the mortality was 15.4 per cent. Seventeen patients had 2 or more lobes removed and the mortality was 80 per cent.

So far as pneumonectomy is concerned, this was carried out in 9 patients and the mortality was 44 per cent, but it must be added that death occurred only in those who had bilateral disease.

Bradshaw, H. H., and O'Neill, J. F. (1943) *Surg. Gynec. Obstet.*, **77**, 315.

Davidson, M. (1944) *Medical Progress*, p. 67.

Goodale, R. L. (1943) *Arch. Otolaryng.*, *Chicago*, **38**, 148.

Simonton, K. M. (1943) *Ann. Otol.*, *etc.*, *St. Louis*, **52**, 598.

BRONCHITIS AND BRONCHO-PNEUMONIA

BRONCHO-PNEUMONIA

Treatment

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Sulphapyridine and similar compounds are most valuable therapeutic agents in acute infections of the respiratory tract and should be prescribed in certain cases of broncho-pneumonia and acute bronchitis, except in very acute infections, it may be advisable to withhold the drug for from 48 to 72 hours after the onset, with the idea of allowing the processes of natural immunity to begin. The drug should be prescribed in adequate dosage, an average adult requires an initial dose of 2 grammes followed by 1 gramme every 6 hours until the temperature falls, and then 0.5 gramme every 6 hours for from 3 to 5 days. Infants tolerate the drug well and require rather a larger dose per body weight than do adults.

Primary atypical pneumonia

Aetiology

It has been clear to clinicians that within the past 30 years there has been a change in certain aspects of pneumonia. Especially from 1937 to 1943 a spate of literature has developed all on the subject of the unusual type of pulmonary response to an aetiological agent which is not yet quite determined. Many names have been employed, additional to primary atypical pneumonia, and thus the nomenclature becomes somewhat confusing if this is not appreciated when terms such as pneumonitis, disseminated focal pneumonia, acute diffuse bronchiolitis, virus pneumonia, benign broncho-pulmonary inflammation, acute interstitial pneumonia, unresolved pneumonia, delayed resolution, silent pneumonia or chronic pneumonia are used. Apart from the profligacy of title there are other evidences which show

BRONCHITIS AND BRONCHO-PNEUMONIA—BURNS AND SCALDS

that the cause of the disease is ill understood, in fact primary atypical pneumonia represents a category in which the classical primary pneumonias cannot be included. There is no doubt that various infective agents are responsible but in the words of Meakins 'no studies reported up to date (April, 1943) have established a clear-cut virus aetiology for this class of broncho-pneumonia'. The American medical service refer always to primary atypical pneumonia by adding 'aetiology unknown'. The possibilities are that the viruses of psittacosis, vaccinia, variola, measles, influenza and varicella—to mention but a few—are the responsible factors in the setting up of atypical pneumonia in specific cases, but no general conclusions can be drawn or particular statements made with regard to the aetiology of the disease.

Clinical picture

The onset is gradual, the symptoms are mild or moderately severe, constitutional manifestations predominate. The chief complaint is cough, usually dry and hacking, about 13 per cent of patients have a sputum. Roughly one-third complain of pain, tightness and discomfort of the chest, most of the discomfort is in the front of the chest, behind the sternum. A very important point is that about 40 per cent in one series had all the signs and symptoms of a cold in the head and chest—a syndrome practically identical with severe coryza. The physical signs in the lungs are very slight. The temperature almost invariably falls by lysis, about 75 per cent of patients have a mild leucocytosis. The disease has run its course by the end of 3 weeks. It is emphasized by all who have dealt with the condition that X-ray examination is essential to diagnosis. The typical hazy type of infiltration spreading out in a fan-shaped manner from the hilar region can be demonstrated. The course is from 5 to 14 days and complications are very rare. In the words of the American Commission which investigated an outbreak, 'the prognosis is excellent'. Treatment by chemotherapy is disappointing.

Meakins, J. F. (1943) *Canad. med. Ass. J.*, 48, 333.

Report of Commission for Investigation of Atypical Pneumonia
(1943) *War Med.*, 3, 223.

BRONZING OF THE SKIN

Corrigendum

In Vol II on p. 716, para. 4, *Pregnancy*, the fourth sentence should read as follows. It may also occur in association with disease of the female genital organs (chloasma uterinum), and is then probably the result of absorption of ovarian hormones, which can produce it experimentally in animals (Bloch and Schraff).

BURNS AND SCALDS

TREATMENT

Aims of treatment

Franklin has summed up the aims of treatment under 3 headings as follows: (1) To prevent the death of the patient by controlling or making good the fluid loss and by preventing if possible the occurrence of that much criticized but very conveniently named condition of 'shock', (2) to anticipate and when possible to prevent infection, (3) to minimize as far as is possible any resultant deformity.

General

The Department of Health for Scotland issued a memorandum (Memorandum No. 8) on the hospital treatment of burns, in which they are classified simply as superficial or deep. The constitutional effects are: (1) primary shock, lasting up to 2 hours, (2) secondary shock, developing 30 minutes after the injury and lasting up to 12 hours, (3) acute toxæmia, which may develop after 6 hours and may last for 60 hours, (4) bacterial toxæmia, developing after 24 hours. These effects may overlap one another. The principles of the treatment include restorative measures for shock, and transfusion of plasma or serum, subsequent transfusions for anaemia and toxæmia, chemotherapy, which is of great value when infection occurs. A high protein and high salt diet and the administration of vitamin C are advocated. Local treatment depends on the site and extent of the burned area. In all cases there is preliminary cleansing under general anaesthesia. Vesicles on the hands are aspirated and the hand is suspended to reduce oedema, coagulation treatment, if used, must be performed with great care. Cod-liver oil emulsion or glycerin-sulphonamide paste dressings are recommended as being simpler to use than saline packs or baths. Burns of the face, except on the eyelids and lips where Vaseline is used, are treated by coagulation. If the scalp is involved the area should be shaved well beyond the lesion to prevent sepsis. For eye burns liquid paraffin drops should be used at once, with subsequent irrigation, and the instillation of atropine drops. Burns of the air passages may necessitate tracheotomy. Burns in other parts of the body may be treated by tanning, by dyes, by oils and emulsions, by saline packs and baths, by the Bunyan-Stannard envelope, by glycerin-sulphonamide paste, by primary excision and skin grafting, or by treatment in closed plaster. For most cases coagulation is recommended if the patient is seen

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within 48 hours, if sepsis develops under a coagulum the latter must be removed and the injury is then treated as an infected wound. Other methods increase the risk of infection and the patient requires more constant care.

The Bunyan bag—The Bunyan bag method was introduced to obviate the pain of adherent dressings and to overcome sepsis. This bag is transparent, very loose fitting, and is sealed on to the skin of the limb after application. It has an inlet and outlet tube permitting irrigation with any fluid—the one used is electrolytically prepared sodium hypochlorite 1 per cent strength. Progress can be observed through the bag and the amount of irrigation required determined. Excellent results are claimed for this method. An objection is the amount of supervision it requires.

Various other forms of treatment—Oily dressings, olive oil and caron oil still have advocates.

Blood plasma and shock—Blood plasma is extensively used in the shock treatment of burns. It is correct in theory, but if not available whole blood transfusion is excellent, when both are impossible intravenous gum saline is useful.

Penicillin and propamidine—The problem of counteracting the effects of haemolytic staphylococci and streptococci from infective burns has been solved to a certain extent by Clark, Colebrook, Gibson, Thomson and Foster, who avoided use of sulphamylamide powder because of its toxic properties in certain circumstances. If penicillin is applied as a powder it produces too much pain, a solution of penicillin is not satisfactory, but when penicillin is made up with lanette wax and castor oil it can be applied thickly as a cream 4 times with intervals of 48 hours between each application. In 76 per cent of cases streptococci disappeared for good within 5 days.

So far as propamidine is concerned a 0.1 per cent cream in a Mumford base was used. Four or 5 applications were made in all, 48 hours being allowed to elapse between each treatment. As with penicillin the burns became free of streptococci within 5 days but only 62 per cent responded. In 8 cases the organism persisted but afterwards was destroyed by application of penicillin. Rapid healing is the rule.

Clark, A. M., Colebrook, L., Gibson, T., Thomson, M. L., and Foster, A. (1943) *Lancet*, 1, 605.
Franklin, R. H. (1944) *Practitioner*, 152, 167.
Memorandum No. 8 (1942) *Emergency Medical Service* H.M. Stationery Office.

CANCER

PATHOLOGY AND AETIOLOGY

Main carcinogenic factors

General review of the aetiology

212 The inherited tendency to develop cancer is not a characteristic of an animal's cells in general but it is confined to one particular organ or tissue. This conclusion has been reached after exhaustive investigations of cancer strains in animals. So far as human beings are concerned there is a strong resemblance to this syndrome. For instance if one of a pair of identical twins has cancer the other in at least 50 per cent of cases is likely to be affected. Some additional factor is probably required in all cases to start the process of cancer in a person susceptible to it. With regard to carcinogenetic substances, the mode of action of these is undetermined.

Most of the recent work on cancer is on the aetiological side and the influence of oestrogenic hormones has been investigated, some connexion has been established between the development of cancer of the breast in individuals who are predisposed hereditarily to the disease, the hereditary disposition is not accepted as an aetiological factor. The hypothesis that there is an infective agent has been accepted by very few.

Extra-chromosomal influence in the transmission of mammary tumours of mice

Bittner¹ and other members of the staff of the Roscoe B. Jackson Memorial Laboratory advanced the hypothesis that mammary tumours in mice were determined by an extra-chromosomal influence. This has been confirmed by many observers.

Further research has proved that Bittner's milk factor is present in milk during the entire lactation period (Andervont and McEleney) and that suckling mice can accept, or are susceptible to, the agent at any period during lactation (Andervont). When new-born mice of a high cancer line are permitted to ingest only a small amount of the agent in milk, it has been found that the incidence of tumours in descendants of these incompletely fostered females tends to decrease with each generation (Bittner²). Andervont has found that the agent survives through 2 generations of the low cancer strain. The agent is present in the thymus gland, spleen and lactating mammary gland of high cancer line mice (Bittner³) and in the blood of normal high cancer strain male and female mice (Woolley, Law and Little). Bittner⁴ has obtained the agent from dried tissue of a spontaneous mammary cancer of the mouse. Experiments with the ultra-centrifuge by Visscher,

Green and Bittner have shown that the agent is very small and may be a 'colloid of high molecular weight' similar to many viruses

DIAGNOSIS

Dangers of delay

The general practitioner and cancer

It is established without a doubt that one of the chief reasons for the high death rate of cancer is delay in having the patient thoroughly examined and the necessary treatment promptly applied. Suggestions have been given by Harms, Plaut and Oughterson who showed that only about 2 per cent of patients with cancer consult a medical man within a month of the onset of symptoms. In 92 per cent of cases there was a delay of 2 months or longer and in 84 per cent a delay of 3 months or longer. The alarming statement is made that the average interval between the onset of symptoms and the beginning of appropriate treatment is 8.46 months. In just over half the number of cases the patient himself or herself is responsible, the doctor being the culprit in 17.4 per cent, there is a joint responsibility in about 28 per cent of cases. Ignorance on the patient's part has been blamed for this delay but with education as it is today and information about cancer freely available it has been suggested that the delay referred to above might be halved if patients knew more about cancer.

TREATMENT

Gye in a personal communication sums up the therapeutic situation with regard to cancer by saying that 'in spite of the great increase of our knowledge of cancer causation, no corresponding fundamental therapeutic advances have been made'.

THE CANCER ACT, 1939

The Act makes the local authorities responsible for seeing that there are adequate facilities for the diagnosis and treatment of those suffering from cancer. The local authorities must consult voluntary hospitals and their medical and surgical staffs, and medical practitioners, with the object of supplying these facilities. A Government grant is available to cover approximately 50 per cent of the increase in expenditure over that incurred in the year ended 31st March 1938. Under the Act only local authorities and voluntary hospitals may advertise the giving of treatment or the giving of advice to those suffering from cancer, except where the advertisement is issued to prescribed persons, for example Members of Parliament, the professions, students and suppliers of surgical appliances. Radium centres for treatment are already established in most parts of the country, but more beds are needed for the reception of those requiring in-patient treatment. The Act provides for free diagnosis but the cost of maintenance in hospital has to be recovered from the patient. Parry urges that the diagnosis and treatment of cancer should not become too regionalized, because it is often possible for a small area to take advantage of the increased facilities offered by a larger one.

- Andervont, H. B. (1941) *J. Nat. Cancer Inst.*, **2**, 13, 307.
- and McEleney, W. J. (1939) *Publ. Hlth Rep., Wash.*, **54**, 1597.
- Bittner, J. J. (1936)¹ *J. Hered.*, **27**, 391.
- (1939)² *Publ. Hlth Rep., Wash.*, **54**, 1827.
- (1940)³ *J. Nat. Cancer Inst.*, **1**, 155.
- (1941)⁴ *Science*, **93**, 527.
- Gye, W. E. (1943) Personal communication.
- Harms, C. R., Plaut, J. A., and Oughterson, A. W. (1943) *J. Amer. med. Ass.*, **121**, 335.
- Parry, R. H. (1939) *J. R. Inst. publ. Hlth Hyg.*, **2**, 629.
- Visscher, M. B., Green, R. G., and Bittner, J. J. (1942) *Proc. Soc. exp. Biol., N.Y.*, **49**, 94.
- Woolley, G. W., Law, L. W., and Little, C. C. (1941) *Cancer Research*, **1**, 955.

CARRIERS IN INFECTIVE DISEASE

TYPICAL RELATIONS BETWEEN CARRIERS AND PARASITES

Relations of carriers to epidemics

Investigation of human infectivity

The range of infectivity has long been known to be restricted in most instances to the immediate vicinity of an infected subject, and the standard 12-foot inter-bed spacing of fever hospitals is based on well tried experience that it constitutes a reliable bacteria barrier, but it is inadequate for virus infections, particularly measles and chicken-pox. The critical range depends on variables such as the degree of infectivity and the amount of catarrh in the individual, on the velocity of expulsion of the *materies morbi*, on whether or not the subject is breathing quietly, is speaking or coughing, on the air currents and ventilation of the atmosphere and the height

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and distance of the infector, as well as on the measures he may take to limit the dispersal of organisms. Careful use of the handkerchief almost entirely arrests the escape of droplets and a cellulose acetate mask also arrests nearly all. A good gauze mask was found to serve efficiently for one sneeze only, and the conventional hand over the mouth was considered to be useless—not more than a polite gesture. The perfect mask has yet to be invented. Impermeable masks either merely deflect the direction of droplets or are found to be too stuffy for prolonged use. The majority of workers still favour gauze masks made of varying thickness but rarely make tests of their efficiency. Rooks, Cralley and Barnes investigated the protective coefficient of different types of masks, which coefficient they found to depend on filtering power in relation to resistance to air flow. They concluded that a mask consisting of 6 layers of gauze, which had been laundered 20 times, filters 97 per cent of organisms and has relatively low resistance to air flow.

Significance of carriers

The relevant problems of the mechanism and possible consequences of infection and cross-infection have been reviewed by Miles who stressed the importance of the carrier state, he pointed out that the nasal passages of the new-born child are sterile but that after 2 weeks 90 per cent of infants in hospital are infected with *Staphylococcus aureus*, in young children the percentage falls to from 50 to 60 per cent and in adults to from 20 to 40 per cent. A further contribution was made by the same author in collaboration with McKissock and Wright who, in addition to reforming hospital ward and operating theatre routine, introduced a new 'non-touch' technique of dressing surgical wounds. This was elaborated in a comprehensive system in a special Medical Research Council War Memorandum, to which the reader is referred for details. Thomas and van den Ende prevented cross-infection by allaying dust by treating floors with spindle oil, and by treating bedclothes with 30 per cent paraffin in white spirit.

McKissock, W., Wright, Joyce, and Miles, A. A. (1941) *Brit med J*, 2, 375

Medical Research Council (1941) *War Memorandum No 6* London

Miles, A. A. (1941) *Lancet*, 2, 507

Rooks, R., Cralley, L. J., and Barnes, M. E. (1941) *Publ Hlth Rep, Wash*, 56, 1411

Thomas, J. C., and van den Ende, M. (1941) *Brit med J*, 1, 953

CATARACT

ACQUIRED CATARACT

Symptomatic cataract

Diabetic cataract

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Aetiology—According to Lawrence, Oakley and Barne a characteristic finding in diabetic coma is temporary opacification of the lens. The pattern observed is of the gridiron type with waves running through it, giving the impression that the capsule is wrinkled in folds, the opacities may also take the form of lines, streaks and so on. Dehydration of the lens may be said to be at the basis of the condition and accounts for the alteration in the appearance of the structure, such dehydration is in accord with loss of fluid elsewhere in the body. It has not yet been determined how long it takes for the lenticular changes to occur after dehydration has begun. Administration of salines is effective if it is made early, but the characteristic changes may become permanent if the disease is allowed to go on for too long. Dehydration of the lens is one factor in the establishment of permanent diabetic cataract of the acute juvenile type but its importance is not so great in adults.

Lawrence, R. D., Oakley, W., and Barne, I. C. (1942) *Lancet*, 2, 63

CELLULITIS

TREATMENT

Vol III

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Sulphonamide drugs have been widely employed in cellulitis, and in many cases have been reported to improve the clinical condition within 48 hours. The prophylactic administration of the drug in the treatment of infected and dirty wounds has also been strongly recommended.

CEREBRO-RETINAL SYNDROMES OF THE HEREDO-DEGENERATIVE TYPE

CLINICAL TYPES

Anomalous types

Comparison of infantile and juvenile types

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Wyburn-Mason sums up the findings after an extensive review of 27 cases and of many other factors associated with amaurotic idiocy and states that there are 2 distinct types of this disease as follows: (1) There is the infantile type, mainly confined to Jews, generally rapid and fatal and occurring before the child is 3 years of

age The cherry red spot may not be seen but there is optic atrophy This condition has a close relationship to the Niemann-Pick disease (2) There is the juvenile type of amaurotic idiocy, which generally begins when the child is from 6 to 8 years of age, but it may appear as early as the second year or as late as the twenties Here Jews are not affected as a rule and the course is much slower, with optic atrophy rather than with pigmentary change Finally there is retinitis pigmentosa

These conditions are not related to each other except that they have similar histological pictures and it is very probable that the disease does not have any connexion with the condition of macular heredo-degeneration

ALLIED CONDITIONS

The Laurence-Moon-Biedl syndrome

Sorsby, Avery and Cockayne review the new information on this syndrome reported between 1935 and the end of 1938 During this period 3 cases were reported from Japan and one from Egypt, whereas all previous patients have been of the Caucasian race Necropsy findings have been reported in 3 cases, and preliminary notes in 2 others, but no significant lesion has been found The range of clinical symptoms and associated conditions are discussed, and the information concerning the inheritance of the condition and the 2 hypotheses regarding its causation are summarized (1) that one gene produces all the signs, and that incompleteness of the syndrome is due to the action of modifying genes and (2) that the syndrome is determined by 2 or more genes Support was given to the hypothesis that the condition is determined either by 2 recessive genes on the same chromosome, or by some chromosomal error such as a dislocation or translocation

Macular dystrophy

Sorsby, in an extensive review of macular dystrophies, concluded that they present such a protean range of manifestations that the classification suggested by Behr is too schematic The range of ophthalmological appearances extends from faint mottling of the macular zone to the picture seen in 'Doyle's choroiditis', almost every possible intermediate lesion having been reported There may be present not only extensive perimacular involvement, but also peripheral lesions, and even some general involvement of the whole fundus The age of incidence extends as do the ophthalmological appearances over a continuous unbroken range

The symptoms also have an equally wide range, they may be so severe as to constitute total day blindness (total colour blindness), or so mild that vision is hardly affected The condition is not necessarily rapidly and relentlessly progressive

Sorsby, A (1940) *Brit J Ophthalm*, 24, 469

— Avery, H, and Cockayne, E A (1939) *Quart J Med*, 8, 51

Wyburn-Mason, R (1943) *Brit J Ophthalm*, 27, 145

CEREBROSPINAL FEVER

TREATMENT

Results of sulphonamide treatment

Sufficient time has now elapsed to allow substantial records to be made and examined with regard to the treatment of cerebrospinal fever by chemotherapeutic methods, especially with regard to the sulphonamides Harries¹ & reviewed 500 cases, Joe reported on a similar number, Jubb analysed 3,206 cases which occurred between 1913 and 1940, Beeson and Westerman examined the statistics of 3,575 cases from more than 100 hospitals in England and Wales In one series, here quoted as a typical example, the general findings were that the death rate was just under 16 per cent, in this computation deaths occurring within 24 hours of admission to hospital were not taken into consideration In the 5 years 1936-40 the decline of fatal cases is evident in the successive death rates 63.8, 61.2, 50.6, 34.2 and 20.2 In the analysis of the 3,575 patients from hospitals, the death rate was 15.9 per cent The ratio of males and females affected is roughly 6:4 Over 45 per cent of the patients were children under 15 years of age The prognosis still tends to be worse in infants and in those who are over 40 years of age In the treatment 5 different sulphonamide drugs were used—sulphapyridine, sulphanilamide, sulphathiazole, soluseptasine and proseptasine Of the total 570 fatal cases 217 patients, or 38 per cent, died within 20 hours of admission Sulphapyridine was used alone in 86.6 per cent of the cases and with the exception of 19 patients, all received sulphonamides Some form of specific serum treatment was administered to 965 patients but serum does not appear to be beneficial to the effect of chemotherapeutic drugs It is obvious that the death rate is still on the down grade and that chemotherapy alone is the most effective treatment at the moment

Beeson, P B, and Westerman, Ethel (1943) *Brit med J*, 1, 497

Harries, G E (1940)¹ *Lancet*, 1, 522

— (1942)² *Brit med J*, 2, 423

Joe, A (1942) *Edinb med J*, 49, 628

Jubb, A A (1943) *Brit med J*, 1, 501

CHAGAS'S DISEASE

MORBID ANATOMY

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Mazza and others have drawn attention to a tumour formation resulting from cutaneous inoculation of *Trypanosoma cruzi*, to which he has given the name 'chagoma'. Its characteristic pathological lesion is a fat necrosis of the tissue cells, especially of the subcutaneous fat, it is part of the initial inflammatory stage of invasion, and is a manifestation of the colonization of the leishmania forms in the fatty tissue. The primary tumour may later give rise to metastatic swellings spread by the blood stream. About a dozen cases with chagoma have been described. In one case, when a child aged 2 years was first taken ill, the mother had noticed that there was a hard dark coloured prominent area, the size of a chestnut, on the postero-internal aspect of the left forearm. Three weeks later several cutaneous swellings were observed over the left breast and on the left flank. Mazza and Urcelay enumerate the cutaneous lesions of Chagas's disease as follows: (1) invasion of the skin itself, (2) extension to the subcutaneous cellular tissue, (3) intense involvement of the epithelium with destruction and necrobiosis, (4) inflammatory cyto-steatonecrosis, with leishmanial forms of *T. cruzi* in the fat cells, (5) centripetal lymphangitis and nodular formations along the paths of the vessels, (6) subepithelial infiltration with obliteration (*borrormiento*) of the line of distinction of the epidermis and corium.

DIAGNOSIS

The Machado reaction as a diagnostic test has been further examined by Lacorte in Brazil, and by Johnson and Kelser in Panama. Lacorte examined the reaction in 35 patients who were suspected or definitely diagnosed to be cases of Chagas's disease. Positive results were obtained in 68.5 per cent of cases, in 35 control patients, including 30 who gave a positive Wassermann reaction and 5 who gave a negative Wassermann reaction, the Machado reaction was negative in every instance. Lacorte concluded that the Machado reaction, when properly carried out, afforded a valuable method of diagnosis of Chagas's disease.

Kelser introduced a modification of the Machado reaction, the essential feature of which was the use, as antigen, of a culture of the trypanosomes in a beef-peptone-agar medium, to which immediately before use a small quantity of a 0.1 per cent solution of dextrose and a little defibrinated guinea-pig blood were added. This modification of the Machado reaction was tested in more than 400 specimens of serum, including a number from known cases of Chagas's disease in man and animals. It proved positive in all known cases of the disease from which serums were available, and negative when there was no evidence of the disease. Johnson and Kelser made use of this technique in a survey of the incidence of Chagas's disease in Panama. They concluded that the Machado reaction is of distinct value, not only in identifying active cases of Chagas's disease, but in showing the incidence of the infection, past and present.

Johnson, C. M., and Kelser, R. A. (1937) *Amer J trop Med*, **17**, 385.

Kelser, R. A. (1936) *Amer J trop Med*, **16**, 405.

Lacorte, J. G. (1938) *Acta Med, Rio de Janeiro*, **1**, 264.

Mazza, S., and others (1940-41) *Publ Univ B Aires, Mision Estud Pat Reg Argent*, Nos 46, 48, 54.

CHANCROID

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Rosser's skin test

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Smith, in discussing the diagnosis of anal and peri-anal ulcerations, draws attention to a skin test taught him by Rosser of Dallas which is useful when Ducrey vaccine is not available. A small area of skin on one buttock is cleansed and dried and then scarified, after which some of the discharge from the suspected lesion is rubbed in. A corresponding area on the opposite buttock is scarified as a control and protected from contamination by any discharge. In positive cases a typical chancroid develops at the test site in 48 hours. Before modern tests were evolved, a similar test was common to distinguish chancroidal from syphilitic ulcers of the genitals. It had the disadvantage that the resulting ulcer might prove very intractable. Now that chancroidal ulcers are much more controllable than formerly the test may be justifiable when antigens for the Frei and the Ito-Reenstierna tests are not available.

Dmelcos vaccine

In a number of cases of bubo de Gregorio injected into the gland 5 cubic centimetres of dmelcos vaccine. Those due to infection with Ducrey's bacillus swelled and became more painful, in others no reaction occurred.

TREATMENT

Smith has also drawn attention to the value of intravenous injections of 1 per cent mercurochrome, first recommended by Rosser in 1933. The first dose is 2.5 cubic

centimetres, succeeding doses at intervals of 48 hours are increased by 2.5 cubic centimetres. The mercurochrome must be freshly prepared.

De Gregorio recommends for the abortive treatment of chancroidal bubo injections of dmelcos into the gland. The injections are given every 3 or 4 days with a fine needle, and the dosage, starting with 0.5 cubic centimetre, is increased by 0.5 cubic centimetre at each successive injection. The injection is followed by some local reaction which usually diminishes with successive doses, the glands become indurated but in time the condition returns to normal. The treatment is useless after suppuration has begun.

Prevention and treatment

Experimental work

The experimental work of Greenblatt, Sanderson, Mortara and Kupperman holds promise of a great improvement in the prophylaxis of chancroid. Ordinary washing with soap and water and application of a mercurial disinfectant have not been productive of much success, tests have therefore been made on 19 volunteers who have been subjected to inoculation with virulent cultures of *Haemophilus ducreyi*, despite the application of the remedies referred to above. Typical chancroids arose. After sulphonamide powder was applied, however, there was success in 5 out of every 7 cases of another group. Sulphonamide ointment is not so satisfactory but a preparation consisting of 25 per cent sulphanilamide or 25 per cent sulphadiazine, and 25 per cent calomel in a water-basis ointment was successful in inhibiting infective processes in 11 out of 13 persons inoculated. Sulphathiazole by the mouth has more success. Of 40 areas of inoculation made in 4 female volunteers only one proved positive. The doses varied, in some cases an individual was given 2.5 grammes of sulphathiazole for the 2 days immediately after the inoculation, another patient had twice that amount, yet another was given 6 grammes of sulphathiazole a day for 7 days before the inoculation was carried out, a fourth had 3.5 grammes of sulphathiazole on the day before the inoculation and 5 grammes a day for the 2 days immediately after the inoculation. When inoculated areas were left untreated the chancroid lesion soon became apparent, there was only one exception to this. The volunteers concerned were quickly cured by having sulphonamides by mouth, the healing process occupied from 5 to 7 days. The local application of sulphonamide powders to chancroids is not so satisfactory, the lesions clearing up much more slowly.

Prevention of chancroid

A number of observers have confirmed that sulphathiazole is very active in the prophylaxis of chancroid, various types of dosage are adopted, in one case 2 grammes of sulphathiazole was given a few hours after the exposure to the disease and a further 2 grammes was given 5 hours later. In a group of 1,400 negro troops Loveless and Denton had good results with a system of giving 2 grammes of sulphathiazole to all those on leaving barracks, 2 grammes on return later on in the evening and 2 grammes early next day. Dealing with those who took the full course the authors report that the incidence of chancroid was only a little over 0.5 per cent per annum as compared with 1.3 per cent in a group of controls, numbering 4,000 soldiers.

Greenblatt, R. B., Sanderson, E. S., Mortara, F., and Kupperman,

H. S. (1943) *Amer J Syph*, 27, 30.

de Gregorio, E. (1938) *Bull Soc franç Derm Syph*, 45, 1746, 1748.

Loveless, J. A., and Denton, W. (1943) *J Amer med Ass*, 121, 827.

Smith, T. E. (1938) *Trans Amer proctol Soc*, 39, 153.

CHICKEN-POX

AETIOLOGY

The virus of herpes zoster has been implanted in the rabbit testis by Kin, and when transferred to susceptibles by subcutaneous injection has produced a febrile reaction with a localized vesicular eruption. Individuals convalescent from chicken-pox and herpes were alike insusceptible to inoculation, indicating that both diseases conferred immunity, not necessarily to the same degree, against the testis-passaged herpes virus.

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PATHOLOGY

Morbid anatomy

Except for the external appearances the changes in chicken-pox are rarely viewed, but Johnson was able to conduct a complete necropsy on a child aged 7 months, who died of hydrocephalus, and had chicken-pox lesions of 3 days' standing at death. Changes closely resembling the cutaneous lesions were found in the oesophagus, liver, pancreas, renal pelvis and adrenals, bladder and ureters, the essential changes were ballooning of the cells, rarefaction and vacuolation of the cytoplasm, and rarefaction of the nucleus with a peripheral position of the nucleolus and nuclear chromatin. In the nucleus there was an acidophilic inclusion body. Capillary damage with haemorrhage and thrombosis was widespread.

Johnson, H N (1940) *Arch Path*, **30**, 292
Kin, O (1939) *Jap J Derm Urol*, **46**, 133

CHILBLAINS

DEFINITION AND AETIOLOGY

- 230 Although Lewis has stated that chilblains and erythrocyanosis crurum puellarum are essentially similar to trench foot Ungley and Blackwood have found that persons susceptible to chilblains do not necessarily suffer from immersion foot when they are exposed to conditions which might give rise to the latter It has to be borne in mind that the histological changes in trench foot are not clear It has been established beyond doubt that the cold which causes chilblains is a damp cold rather than the dry, frosty type of cold Those who suffer from chilblains probably have skin capillaries which are affected beyond normal by spasm, such vessels do not relax in the ordinary way after vasoconstriction of the vessels of the legs is produced by cold Thus the capillary walls are subjected to a lengthened period of anoxia and they become more permeable

TREATMENT

There is evidently quite a considerable amount of unsatisfactory treatment in vogue Parathyroid tablets are useless, calcium is very much overrated and vitamin D has no claims for support as a therapeutic agent Physiotherapy is most satisfactory, especially in the form of galvanic baths

Lewis, T (1941) *Brit med J*, **2**, 837
Ungley, C C, and Blackwood, W (1942) *Lancet*, **2**, 447

CHOLERA

EPIDEMIOLOGY

- 235 The importance of the presence of O subgroup I antigen in the true cholera vibrios is confirmed by Taylor in a valuable summary of the work on the subject This heat-stable O antigen can be preserved in a dry form and used for serological tests of isolated vibrios The 2 main subtypes of *Vibrio cholerae* were used, namely the 'original' or Inaba and the 'variant' or Ogawa strains, each of which contains a common O antigen in addition to its own specific one It has now been established that the incidence of vibrios inagglutinable with O group I serum in cases of clinical cholera is no greater than in the general population of an area, so such are mere accompaniments of the true cholera vibrios and are intestinal inhabitants as much of the non-cholera as of the cholera population Moreover, the true cholera vibrio as above defined has not been isolated except in immediate relation to cholera cases The cholera convalescent and contact carriers in most cases are free from the causative vibrio after 5 days from the onset of the attack or contact with a connected case Further the *V. cholerae* does not apparently persist in water for more than a maximum of 16 days Thus cholera cases are the major factors in disseminating the disease and maintaining endemicity, and close contact carriers and water sources infected from a case act as intermediaries for short periods only and at short range

It may be noted that the above facts are in accordance with the conclusion derived from a comprehensive study by Rogers of 60 years' Indian cholera records, namely that the movements of pilgrims do most to spread cholera in India

Panja, Malik and Paul record having found the *V. cholerae* in the vomit induced by giving sterile water to drink in 26 out of 52 examinations, especially when the pH of the fluid was above 6.0 but not when it was below 5.0 The amount of sodium chloride in the vomit varied widely between 66 and 821 milligrams in 100 cubic centimetres

BACTERIOLOGY

Venkatraman and Ramakrishnan advise the use of a medium, prepared in the following way, for the preservation of cholera vibrios in stools that have to be sent to a distant laboratory for making cultures Boric acid, 12.405 grammes, and potassium chloride, 14.912 grammes, are dissolved in about 800 cubic centimetres of water (not distilled), the solution is cooled and made up to 1 litre Two hundred and fifty cubic centimetres of this stock solution are mixed with 133.5 cubic centimetres of N/5 sodium hydroxide solution and the whole is made up to 1 litre Twenty grammes of common salt are dissolved and the buffered saline is filtered through paper, dispensed in 10 cubic-centimetre quantities in 1 ounce screw-capped bottles and sterilized in an autoclave A small aluminium spoonful (1 to 3 grammes) of the stool, according to its consistency, is added and is well mixed before being despatched to the laboratory The pH of the medium is 9.2 and cholera vibrios have been preserved in it up to 92 days without alteration of the pH In a trial in the field the culture results were almost the same as those from cultures which were made on the spot with the fresh stools

Read and Pandit have studied the occurrence of the non-haemolytic *V. cholerae* agglutinable with pure O serum and of the haemolytic El Tor strains in rural areas in India They found the former in all but one of clinical cases of cholera,

in 7 per cent of close contacts of such cases and in about 16 per cent of water sources in direct contact with cholera cases, but the vibrios did not persist for much over a fortnight. On the other hand, the El Tor vibrio was detected in areas usually in the absence of cholera and in relatively large numbers in an area which had been free from cholera during the previous decade. These findings are contrary to recent reports from Celebes.

Venkatraman and Ramakrishnan also deal with the occurrence of the El Tor vibrio in natural sources of water in the absence of cholera in view of the Celebes reports. From an experience of bacteriological examinations of 1,827 stools and 237 natural sources of water they conclude 'The isolation of haemolytic agglutinable vibrios (*V. El Tor*) from 15 open natural water sources in 2 rural areas in the absence of cholera is recorded'.

PATHOLOGY

Changes in the blood in cholera

Pasricha and Malik confirm the well known increase in the volume of erythrocytes and in the percentage of haemoglobin, together with a decrease in the concentration of sodium chloride in some cholera cases. They also report an increase in urea and non-protein nitrogen, in the total plasma proteins, fibrin and globulin fractions and in glucose. Chatterjee and Sarkar record very similar results and emphasize the great concentration of the blood due to dehydration, together with acidosis, which are so important as a guide to treatment by hypertonic and alkaline salines. They also found diminished sodium with increased potassium content and lowering of serum calcium, and noted a decrease in blood sugar in most cases. Banerjee² notes that the excessive vomiting and diarrhoea of cholera lead to great loss of chlorides, this they estimate at 9.7 grammes of chloride through vomiting and 34.6 grammes by the bowel in 24 hours, with consequent hypochloræmia, dehydration from loss of fluid, retention of nitrogenous waste products and renal failure. Banerjee³ also stresses the occurrence of congestion of the kidneys—especially of the glomeruli—as part of the systemic peripheral capillary failure, accompanied by engorgement of the splanchnic area, producing failure of the kidney functions. Pasricha and Malik have also described methods of estimating the chemical constituents of the blood, using quantities of 4 cubic centimetres at a time.

PROGNOSIS

Turnbull confirmed the low mortality in the resistant Chinese, following the use of the hypertonic and alkaline salines intravenously. In an outbreak of cholera in southern China among hospital cases which were of a severe type the mortality in from 400 to 500 cases was only from 8 to 8.75 per cent.

TREATMENT

Anticholera inoculation

Taylor, Ahuja and Singh found that cholera vaccines would keep for 2 years in a hot climate. To produce effective immunity 5 to 6 days were required, but the immunity was higher after 8 to 10 days.

Saline transfusions

Banerjee⁴, in an experience of 1,000 cases treated with the standard alkaline isotonic and hypertonic salines, using freshly sterilized tap water, advises that the temperature of the solutions should be as much above 98° F. as the rectal temperature is below it in order to prevent severe reactions with rigors. If the rectal temperature is high before the injection it should be reduced by an enema of from 15 to 20 ounces of ice-cooled physiological saline.

Panja, Malik and Ghosh found that severe rigors and pyrexia after the giving of hypertonic salines in cholera can be much reduced in frequency by using pyrogen-free distilled water as the solvent. This they obtained by redistillation in an all-glass still in the presence of a few drops of sulphuric acid and a few crystals of potassium permanganate to produce a faint pink colour. For the same purpose, Tui and Wright advise the use of filtration through compressed asbestos pads, the equipment for which cost 1,000 dollars. Several thousand litres were used without any febrile reactions.

Sulphonamides

Sulphaguanidine in the treatment of cholera has been tried by Carruthers in an initial dose of 0.1 gramme per kilo weight, followed by 0.05 gramme per kilo every 4 hours, in addition to the routine hypertonic saline and alkalis given orally. No toxic symptoms were noted, but it was concluded that the new drug did not possess any value in this disease. By laboratory studies of the effects of sulphonamide drugs on *V. cholerae* Griffiths, on the other hand, with the use of smaller infective doses of the *V. cholerae* than were used by previous workers, injected intraperitoneally in mice, found that a single injection of sulphathiazole or sulphadiazine given one-half to one hour after the infecting dose greatly reduced the death rate of the animals. The value of sulphonamide treatment of cholera is thus unsettled as yet.

CUMULATIVE SUPPLEMENT 1945

- Banerjee, D N (1938)¹ *Arch Schiffs- u Tropenhyg*, **42**, 543
— (1941)² *Indian med Gaz*, **76**, 345
— (1941)³ *J Indian med Ass*, **10**, 443
Carruthers, L B (1942) *Trans R Soc trop Med Hyg*, **36**, 89
Chatterjee, H N, and Sarkar, J (1941) *Trans R Soc trop Med Hyg*, **34**, 379
Griffiths, J J (1942) *Publ Hlth Rep, Wash*, **57**, 814
Panja, G, Malik, K S, and Ghosh, S K (1942) *Indian med Gaz*, **77**, 282
— — and Paul, B M J (1942) *Indian med Gaz*, **77**, 347
Pasricha, C L, and Malik, K S (1940) *Indian J med Res*, **28**, 301
Read, W D B, and Pandit, S R (1941) *Indian J med Res*, **29**, 403
Taylor, J (1941) *Cholera Research in India 1934-1940 under the Indian Research Fund Association A Review* The Job Press, Cawnpore, pp 1-88
— Ahuja, M L, and Gurkirpal Singh, J (1936) *Indian J med Res*, **23**, 609
Tui, C, and Wright, A M (1942) *Ann Surg*, **116**, 412
Turnbull, T A (1938) *J R nav med Serv*, **24**, 138
Venkatraman, K V, and Ramakrishnan, C S (1941) *Indian J med Res*, **29**, 681

CHOREA

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DEFINITION

Although chorea should, in the present state of knowledge, be regarded as a form of rheumatism, because statistically from 50 to 70 per cent of the cases show evidence of rheumatism at the time, or within 5 years of the attack, it cannot so easily be accepted that chorea, *per se*, suffices for the diagnosis of rheumatic activity, because the temperature and especially the blood sedimentation rate are usually normal in uncomplicated cases

Pathogenesis

The origin of the choreic* movements has given rise to much speculation, many believe that there is some dysfunction of the cerebral cortex and the use of the electroencephalogram has supported such contentions Buchanan, Walker and Case are of the opinion that the motor area is the region directly responsible for the production of the choreic movements, when this area is stimulated by an electrical current motor movements of choreiform type are produced On the other hand, the pathological investigation of the brain of choreic subjects shows that the lesions are not confined to the cerebral cortex but may also extend to the cerebellum and afferent paths in the striatum and in the thalamus Indeed it has been proved that there are 2 subcortical circuits which may influence the activity of the cerebral cortex, one is the cortico-ponto-cerebello-dentato-rubro-thalamo-cortical circuit, the second is the cortico-strio-thalamo-cortical circuit, any alteration in the mechanisms of these circuits must affect the sensitivity of the motor cortex It should also be borne in mind that the cerebral cortex is not of the same degree of excitability in every case Buchanan, Walker and Case, while they believe that choreiform movements originate at the level of the cerebral cortex, nevertheless consider that the cortex must be hyperexcitable, this condition may be the result of congenital abnormalities or of functional gaps in the circuits which regulate the activity of the cortex

AETIOLOGY

Like all rheumatic conditions, chorea is prone to relapse, but, if the heart escapes damage in the first attack of chorea, it is more likely to remain unaffected in later attacks

TREATMENT

Drugs

Salicylate is still the drug of choice in Great Britain but it is of doubtful therapeutic value Arsenic is little used and sulphanilamide has been tried without any success Of sedatives used Drucker from the University of Copenhagen has had encouraging results from the giving of large doses of luminal He recommends 10 centigrams 3 times a day for 14 days or until a rash appears—usually about the ninth day The dose is then reduced to 5 centigrams 3 times a day for 4 weeks and then 5 centigrams twice daily for 4 weeks Fluids only are given during the first massive dose More than three-quarters of the cases were symptom-free within 3 weeks as compared with only 7.5 per cent of the control cases

Pyretotherapy

Pyrexial therapy has had little trial in Great Britain, but is strongly advocated by several American authors, although others doubt its lasting value The fever can be induced by typhoid vaccine or by electrotherapy Vian recommends T A B

vaccine intravenously The initial dose is $\frac{1}{2}$ cubic centimetre increasing by $\frac{1}{2}$ cubic centimetre daily Improvement usually occurs after 3 or 4 doses Krusen and Elkins recommend physically induced therapy A course of 10 or 12 sessions of between 2 and 3 hours daily at which the body temperature is maintained at 104° to 105° F is recommended

Buchanan, D N, Walker, A E, and Case, T J (1942) *J Pediatr*, 20, 555

Drucker, P (1939) *Acta paediatr, Stockh*, 26, 98

Krusen, F H, and Elkins, E C (1939) *J Amer med Ass*, 112, 1689

Vian, H (1940) *Un méd Can*, 69, 722

CLIMACTERIC AND ITS DISORDERS

THE CLIMACTERIC IN THE FEMALE

Treatment

Hormone therapy

Oestradiol benzoate can be given by hypodermic injection, by the mouth or in the form of a vaginal suppository, in its crystalline form it may be implanted subcutaneously In well established cases 50,000 international units of oestradiol benzoate, injected intramuscularly, may be given every other day until from 3 to 5 doses have been administered, after that oral tablet medication with 10,000 international units every day for a week or two until the dose is reduced to one of from 3,000 to 6,000 international units in tablets given 2 or 3 times a week It is also essential that the patient should rest and very often sedatives are required Implantation of crystalline oestrone in pellet form in the subcutaneous tissues should not ordinarily be made, this treatment is indicated when the patient may have had a hysterectomy or when she may have been completely over the menopause for several years, the danger is uterine haemorrhage The most suitable type of treatment in this category is the implantation by trocar and cannula of 60 milligrams, the sites chosen being the buttock, rectus abdominis sheath or intercostal region

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CLONORCHIASIS

Erratum

In Vol III, p 255, para 7, line 6 after '300 mgm' insert 'per kilogram of body weight'

PARASITOLOGY

Kawana reported that, in the district of Shanghai, dogs, cats and rats had been found to be reservoir hosts for *Clonorchis* Of 15 house dogs, none was infected, but of 228 'field' dogs 36.6 per cent were infected, 58 per cent of 202 cats were infected

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The fish *Hypomedus olidus* had been found by Ide to act as host for the larval stage of *C sinensis* This fish if eaten raw was therefore dangerous It is the first member of the *Salmonidae* to be incriminated

In experiments with the fish *Pseudorasbora parva*, most of the cysts were found in the region of the terminal vertebrae This suggests that this is the site of election and that larger fish should be examined, particularly in this region (Hsu)

Experiments with 16 dyes *in vitro* showed that gentian violet, malachite green, and Nile blue sulphate in concentrations approximating those used therapeutically killed the worms, gentian violet was the best of the three (Chu)

Kawai administered gentian violet orally to 7 dogs infected with *C sinensis* and estimated the results by egg counts He confirmed the efficacy of this drug, especially for light infections, in which the worms were reduced by 61 per cent in 15 days The dose varied in light cases 18 milligrams per kilo body weight once every 3 days for 15 days to a total dose of 1,200 milligrams, in a moderate case of from 18 to 20 milligrams per kilo body weight daily for 19 days to a total dose of 3,040 milligrams, and in a heavy infection 120 milligrams (from 10 to 12 milligrams per kilo body weight) daily for 45 days, to a total dose of 5,400 milligrams

Chu, H J (1938) *Chin med J*, 54, 409

Hsu, H F (1939) *Chin med J*, 55, 542

Ide, K (1936) *Kitasato Arch*, 13, 40

Kawai, T (1937) *J med Ass Formosa*, 36, 386

Kawana, H (1936) *J Shanghai Sci Inst*, 2, 75

COCCYX DISEASES

FRACTURE, DISLOCATION, AND BRUISING

Fracture

The war has produced quite a number of cases of fracture of the coccyx These fractures may be simple or compound Some of the fractures are produced by bomb fragments, and portions of the coccyx may even be driven into the rectum Armenians have sustained compound comminuted fractures of the coccyx due to bullets fired from below by enemy fighter aircraft Other cases of fracture are due to the patient

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In war injuries

Concussion in head wounds as a rule is slight, or absent, in contrast to that in civil injuries. On the other hand, unconsciousness may occasionally occur late and be prolonged. Again, focal symptoms are more frequent than in civilian injuries. They have a strong tendency to undergo spontaneous recovery, and operation is indicated only when they come on late. By means of ventriculography cases can be separated into those with a good and a bad prognosis.

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TREATMENT

War injuries

The principles of the treatment of head wounds have been laid down by Cairns and Jefferson, and are fundamentally the same as in the war of 1914–18. (1) To remove infective material and dead brain tissue, (2) to remove blood clot, extra-dural or sub-dural, and aerocele, (3) on account of the possibility of epilepsy, to consider if retained foreign bodies should be removed.

The scalp should be opened and closed in 2 layers—galea and skin—using thread, after dusting with a sulphonamide. This may be done for 3 days or even longer, but the important criterion is whether or not the wound is penetrating, leading into the dura, every means should be taken to settle this question. When the dura is opened, damage to nervous pathways, and spread of infection to the ventricles and basal cisterna, and later the occurrence of abscess and possibly epilepsy, must be borne in mind. The dural wound should not be enlarged unless the surgeon is prepared to remove necrotic brain and clot in order to prevent tension. Otherwise fungus of the brain will develop. Forcible irrigation and suction are employed for this, and, at the same time, all dirt, foreign bodies, and detached bone must be removed. In penetrating or tangential wounds, the bone may be nibbled away, or an osteoplastic flap may be raised. The advocates of the latter method claim better access and reduced infection. The general impression is that repair of the dura is unsafe and that tension and fungus can be controlled by repeated lumbar puncture. Gaping wounds may have to be left open unless they can be closed by means of a sliding skin graft. Missiles within the brain are usually left alone, but if the clinical signs are multiplied and if the protein content of the cerebrospinal fluid increases, bold measures must be taken for their removal. There is an impression that sulphonamides, given either by mouth or intravenously, delay the necessity of operation. They tend to localize the infection within the brain and the resultant abscesses can be excised whole with their capsule at a later date.

CONJUNCTIVA, INJURIES AND DISEASES

INFLAMMATION DUE TO BACTERIAL INFECTION

Acute conjunctivitis

Treatment

With a really acute conjunctivitis, presumably of bacterial origin, sulphonamide treatment should be instituted without delay, this may be with sulphathiazole or sulphapyridine. Five grammes a day should be given for 2 days, that is 10 tablets, 0.5 gramme, a day (3 on rising, 2 at midday, 2 at teatime and 3 at bedtime). The tablets should be given crushed in 2 tumblerfuls of water each time. The fluid intake should be 6 or 7 pints a day. The drug may be continued for 2 days more if necessary, then it must be stopped. The best results are obtained when the urine is alkaline, therefore an alkaline mixture containing potassium citrate or sodium citrate 30 grains, potassium bicarbonate 20 grains in a fluid half-ounce of chloroform water should be given 4 times a day. The treatment should be used also in conditions of gonococcal ophthalmia of adults.

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NON-BACTERIAL INFLAMMATION

Inclusion conjunctivitis

Morbid anatomy

Recent evidence from a study by Thygeson and Stone of inclusion conjunctivitis in infants, children and adults, indicates that the reservoir of the virus is a mild genito-urinary infection which is transmitted venereally, in the male the lesion is a low-grade non-gonococcal urethritis, and in the female there is subclinical cervicitis limited to the region within the internal os. Gonorrhoea is commonly present in association with the virus infection, but the 2 infections appear to be independent. The virus infection may be transmitted to the eyes during delivery, or from contaminated water in swimming-baths. In a series of 51 patients (39 infants, 3 children, 9 adults) the disease in the infants was a papillary conjunctivitis, and in the children and adults was mainly follicular hypertrophy. Local treatment with silver nitrate was useless, but sulphanilamide when given by mouth in 18 cases and 5 per cent sulphathiazole ointment in 6 cases resulted in rapid cures.

Treatment

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The value of sulphanilamide by oral administration in cases of inclusion conjunctivitis in infants and adults has been described by Thygeson in previous reports. It was found that infants responded in the first days of treatment and were usually cured within a week. In adults the papillary type of the disease responded equally rapidly but, in cases with predominant follicular hypertrophy, several weeks were required for the conjunctiva to return completely to normal. The inclusion bodies which are characteristic of the disease could not be found after the first few days of treatment. There were not any recurrences in cases in which the treatment was continued for 6 days or longer. Local therapy with the same drug was ineffective.

Since the virus of inclusion conjunctivitis is known to attack epithelium only and its superficial layers most concentratedly (thereby differing *in toto* from trachoma), oral therapy does not appear to have any advantage over local therapy other than that concerned with the maintenance of a constant therapeutic concentration of the drug.

The local use of 5 per cent sodium sulphathiazole ointment applied 6 times daily was effective in causing rapid healing in 11 out of 15 cases of inclusion conjunctivitis in infants, children and adults.

Sorsby, Hoffa and Smellie report that the sulphonamide compounds have proved effective in the treatment of non-gonococcal ophthalmia as well as in the gonococcal type of infection. The results obtained by the use of sulphapyridine are highly satisfactory and constitute a notable advance in treatment. The recommended dosage is usually 0.125 gramme given by mouth, 3 to 4 times daily, local treatment is almost superfluous.

Sorsby, A., Hoffa, Elizabeth L., and Smellie, Elspeth W. (1942)
Brit med J, **1**, 323

Thygeson, P., and Stone, W., Jun. (1942) *Arch Ophthal*, N.Y., **27**, 91

— — (1942) *J Amer med Ass*, **119**, 407

CONSTIPATION**TREATMENT****Management of cases of dyschezia**

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The term, constipation, comprises colonic constipation and dyschezia, the main difference between these two conditions is that the latter does not give rise to auto-intoxication, the symptoms being due to reflex influences. In mapping out the treatment of dyschezia it has to be remembered that most patients reach the doctor's consulting room after many trials have been made of various aperients, these patients do not necessarily require aperients—they have lost the faculty of natural evacuation and they require to be re-educated in good habits. The first essential therefore is to stop aperients and to instruct the patients with regard to general regularity of rectal evacuation. When despite the above, failure is reported, the indication is that the abdomen and rectum should be carefully re-examined and in severe cases an X-ray examination should be made.

The basis of treatment being restoration of the defaecation reflexes which have been neglected or put out of use by the constant taking of aperients, much good may result from frank discussion of the physiology of defaecation with the patient. This may have the desired effect of re-establishing normal evacuation but it may be necessary at the beginning to give a teaspoonful of vegetable mucilage, for example I-so-gel, or from 2 to 4 fluid drachms of liquid paraffin, so that the faeces may be softened or increased in bulk.

CONVULSIONS IN INFANCY AND CHILDHOOD**TREATMENT****Immediate treatment**

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Prompt measures for the treatment of the actual convulsion are more important than is the reaching of an exact diagnosis, which can be made later on. Paraldehyde may be given by rectum, a drachm of paraldehyde being used in 1 ounce of olive oil for each 14 pounds of body weight.

If in infants the fontanelle is tense and there is a suspicion of intracranial haemorrhage or meningitis, lumbar puncture may be performed. This is of value from a diagnostic as well as from a therapeutic point of view. The demonstration of a blood-stained fluid should lead to the giving of vitamin K.

CORNEA, INJURIES AND DISEASES**INJURIES****Gas injuries in warfare***Mustard-gas and the eyes*

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The outstanding work within recent years is that of Mann and Pullinger who performed experiments on the rabbit's eye, the research was carried on for many

months and the results have been used in a comparison with the conditions found in the human eye. The human being when affected by mustard-gas has early symptoms and late symptoms. The former usually run a course of from 12 to 18 months, the latter from 10 to 15 years. It has been possible to induce lesions at the corneo-scleral junction of the rabbit, similar to those found in human beings, these lesions taking the form of characteristic corneal blood islands and varicosities with late ulceration in the cholesterol deposits. The important point is that such lesions cannot be induced by an agent other than mustard-gas, this also holds good so far as the late ocular lesions in man are concerned. The outcome of these researches is that reaction in the eye is dependent upon the site of the lesion and the character of the mustard-gas—droplet or vapour.

Bonnefon's treatment

The somewhat revolutionary methods adopted by Bonnefon in the treatment of mustard-gas injuries of the eyes in 1918 also demands consideration. The essentials of the treatment are osmotic drainage of the affected mucous membrane, an eye bath filled with warm hypertonic solution being used. The lotion consists of a saturated solution of sodium sulphate $1\frac{1}{2}$ pints, and syrupus simplex about one-third of a pint. It is essential to continue the treatment long after the acute stage is past and until photophobia and lacrimation have disappeared.

Bonnefon, G (1939) *Gaz hebdomadaire de médecine*, **60**, 168

Mann, Ida, and Pullinger, Beatrice D (1941) *Proc R Soc Med*, **35**, 229

CORONERS AND INQUESTS

Erratum

In Vol III, page 439, line 12, for 'accident' read 'trauma'

Addendum

On page 439, line 22, add: It is in general useless to ask the coroner (say by telephone) if it is permissible to give a certificate, since the moment he is communicated with he is put on inquiry, and must send his officer to obtain particulars.

CROHN'S DISEASE

CLINICAL PICTURE

In Crohn's series of cases the onset was acute in 11, but symptoms had been present for from 1 to 5 years in 62 patients, for from 5 to 10 years in 15 and for more than 15 years in 8. Signs of obstruction were present in 10 cases only. The tendency to form fistulae was marked. Internal fistulae were present in 11 cases, external (opening into a laparotomy scar) in 12, and peri-anal, rectal and rectovaginal in 20 (some of the tracks were long and circuitous). The prognosis in acute cases varied, some cases appeared to undergo spontaneous cure without resection. Spontaneous regression was not observed in chronic cases.

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TREATMENT

Surgical treatment

Cases of Crohn's disease may be classified into acute, subacute and chronic groups, this is a method adopted by Holloway who is guided only by the gross appearance of the lesion. In the acute stage conservative treatment is recommended. In the subacute stage, resection may be necessary. In the chronic stenotic phase surgical treatment may be successful, primary resection being the operation of choice.

Medical treatment should be restricted to patients in whom operation is impossible owing to the extensive involvement of the intestine. Surgically a higher percentage of permanent cures is obtained from resection than from short-circuiting operations. Among 39 resections there were 3 recurrences, probably owing to the difficulty of recognizing at operation the upper limit of the affected mucosa, this was rendered more difficult by the fact that the inflammatory process is not always continuous, but may be interrupted by one or more 'skip areas', extending as far as 18 inches. The most important post-operative treatment is a high protein diet, with supplementary whole vitamin B complex and foodstuffs with a low residue.

Crohn, B B (1939) *Surg Gynec Obstet*, **68**, 314

Holloway, J W (1943) *Ann Surg*, **118**, 329

CYANOSIS

TREATMENT

Methaemoglobin and sulphonamides

According to Carey and Wilson there is apparently little relation between the dose of sulphanilamide and sulphapyridine and the blood levels of the 'free' amounts of these substances. This may be due to the following factors: (1) Individual variation in the degree of acetylation in the body of these drugs, resulting in varying amounts of 'free' substance, (2) individual variation in absorption from the gastro-intestinal tract may be influenced by the severity of the infection, (3) the time the drug is given in relation to food, (4) the rate of urinary excretion may vary. There seems to be no

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- 278 noticeable relation between increasing amounts of methaemoglobin and increasing blood concentration of free sulphanilamides and sulphapyridines. Methaemoglobinaemia was observed in almost every patient treated with sulphanilamide or sulphapyridine.

Carey, B W, and Wilson, J L (1940) *J Pediat*, 17, 38

CYANOSIS, ENTEROGENOUS

AETIOLOGY

Sulphonamide drugs

- 279 Sulphaemoglobinaemia and methaemoglobinaemia readily occur as the result of treatment with any of the sulphonamide drugs, because these drugs catalyse the reaction between sulphuretted hydrogen and haemoglobin. No deaths have been recorded, and the cyanosis is not considered to be sufficient cause for ceasing this treatment when it is urgently required. Putrefaction, with the formation of sulphuretted hydrogen, occurs when the colon is full of fluid. When sulphonamide drugs are being taken, therefore, saline purges and drastic purges should be avoided, and sulphur-containing foods should be prohibited. Liquid paraffin is the safest laxative.

CLINICAL PICTURE

Blood examination

Fairley reports on studies on methaemalbumin, and describes the spectroscopic appearances and reactions of methaemalbumin in human plasma and in blackwater fever serum, and the differentiation of methaemalbumin and sulphaemoglobin. Methaemoglobin has been previously erroneously described as occurring in the plasma of patients with intravascular haemolysis and haemoglobinuria, through failure to differentiate spectroscopically between methaemoglobin and methaemalbumin. Since methaemoglobin and sulphaemoglobin are essentially intracorporeal, it is suggested that the term methaemoglobincythaemia should be used instead of methaemoglobinaemia, and sulphaemoglobincythaemia in place of sulphaemoglobinaemia. On the basis of Schumm's test, haematinaemia should now be called methaemalbuminaemia. Biochemically the haemolytic anaemias may show (a) hyperbilirubinaemia only, (b) hyperbilirubinaemia and methaemalbuminaemia, and (c) hyperbilirubinaemia, methaemalbuminaemia and haemoglobinaemia.

TREATMENT

The methaemoglobinaemia caused by sulphonamide drugs may be treated by the intravenous injection of methylene blue (0.1 to 0.2 cubic centimetre per kilogram body weight of a 1 per cent aqueous solution) or by the administration of 0.5 to 1.0 grammes per day of methylene blue by the mouth (Wendel).

Fairley, N H (1941) *Quart J Med N S*, 10, 95

Wendel, W B (1939) *J clin Invest*, 18, 179

DARIER'S DISEASE

MORBID ANATOMY

- 282 Peck, Chargin and Sabotka regard the disease as 'a physiological naevus with hereditary weakness in vitamin A absorption, or in conversion of provitamin A to vitamin A'. These authors record 3 cases improved by administration of 200,000 United States Pharmacopeia units of vitamin A given daily by mouth. Improvement under treatment by Grenz rays is reported by Weissenbach, Levy-Franckel and Meyer, and by Jungmann who regards this treatment as the method of choice.

Jungmann, H (1939) *Brit J Derm*, 51, 163

Peck, S M, Chargin, L, and Sabotka, H (1941) *Arch Derm Syph*, N Y, 43, 223

Weissenbach, R J, Levy-Franckel, and Meyer, J (1939) *Bull Soc franç Derm Syph*, 46, 1339

DEAFNESS

TREATMENT

Otosclerosis

Tinnitus aurium

- 284 General treatment is very important, the best drugs are codeine and phenacetin given in small doses. If the blood pressure is low, the elixir ephedrinae hydrochloridici (B.P.C.) is to be recommended, but when it is high, belladonna, preferably in the form of Bellafoline (Sandoz), is recommended. The sodium-free diet has not been a success. Surgical treatment generally is not to be recommended.

DENTAL SEPSIS IN RELATION TO SYSTEMIC DISEASE

CONDITIONS ASSOCIATED WITH DENTAL SEPSIS

Diseases of circulatory system

- 288 Elliott has again called attention to the occurrence of transient streptococcal bacteraemia as a sequel to dental extraction. Acute apical infections are not so

CYANOSIS, ENTEROGENOUS—DIABETES INSIPIDUS

commonly the source of such an invasion as are parodontal infections. Chronic gum infection is especially likely to cause bacteraemia even apart from dental operations, this may result from slight trauma, such as mastication of hard food, brushing the gums, or 'rocking' a tooth. Although this bacteraemia does not usually produce remote ill effects, Elliott considers that subacute bacterial endocarditis may result in patients with pre-existing valvular deformity, either congenital or rheumatic. Elliott reports that, of 56 patients with bacterial endocarditis, 13 dated the onset of their illness from a dental operation, 9 of these 13 were admitted to hospital with fully developed bacterial endocarditis within 8 weeks of the operation, and the others within 6 months. Elliott considers that in patients with any cardiac abnormality scrupulous care should be taken when dental extractions are essential, and 'rocking' a tooth before extraction should especially be avoided.

Barnes and Trueta report experiments showing that bacteria travel from the tissues to the blood in the lymph stream only, even from freshly inflicted wounds, and the above workers also confirm the earlier observations of Elliott.

Dyspepsia and rheumatism

Vaizey and Clark-Kennedy have reviewed the relation between dental sepsis and general diseases (anaemia, dyspepsia and rheumatism). As a result of increased knowledge of the aetiology of anaemia, dental sepsis is no longer regarded as an aetiological factor. As regards dyspepsia, the authors' observations suggest that the loss of the power of proper mastication is a potent cause of dyspepsia, particularly during the period after the teeth have been extracted and the dentures not yet fitted. Of 76 dyspeptic patients from whom the teeth were removed, 6 were benefited, of 126 patients from whom the teeth were extracted for dental reasons, 39 (31 per cent) developed dyspeptic symptoms. The authors consider that the aetiological importance of dental sepsis in rheumatism is equally uncertain. Of the 126 patients whose teeth were removed for dental reasons, 19 (15 per cent) developed rheumatic symptoms.

Barnes, G. M., and Trueta, J. (1941) *Lancet*, 1, 623

Elliott, S. D. (1939) *Proc. R. Soc. Med.*, 32, 747

Vaizey, J. M., and Clark-Kennedy, A. E. (1939) *Brit. med. J.*, 1, 1269

DERMATITIS DUE TO INJURY AND POISONING INCLUDING FEIGNED ERUPTIONS

EXTERNALLY APPLIED AGENCIES DIRECT EXPOSURE

Toxic dermatitis

Contact dermatitis of the feet

Sensitization is on the increase, and dermatitis of the feet as a result of contact with new shoes or stockings has been reported. The signs and symptoms may resemble those of epidermophytosis but there is not any fungus to be found on microscopical examination.

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DESMOID TUMOURS

MORBID ANATOMY

Pearman and Mayo report observations made on a series of 77 cases. In 55 patients the tumour arose in the striated muscle of the anterior abdominal wall, in the other 22 cases it involved striated muscle in other regions. Histological examination is essential for diagnosis.

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Pearman, R. O., and Mayo, C. W. (1942) *Ann. Surg.*, 115, 114

DIABETES INSIPIDUS

TREATMENT

Depot-pituitary

The possibility of using depot-pituitary in the treatment of diabetes insipidus, in a way comparable to the method of using depot-insulin, is suggested in a report of Wankmüller. He treated with satisfactory results 2 patients with diabetes insipidus and 1 with polydipsia after fracture of the base of the skull, with tonephun-depot, an emulsion of posterior pituitary extract in a basis described as plant and animal lipoids. The presence of certain regulating substances, for instance metal ions, controls the passage of the active principles through the cell membranes. The author claims that intramuscular injections have a prolonged effect, up to 5 days, and that with this method the total amount of active substance required is reduced by from 50 to 80 per cent. There were no unpleasant sequelae. If similar results are obtained in trials on larger numbers of patients it will mark an advance in the treatment of diabetes insipidus.

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Wankmüller, R. (1939) *Klin. Wschr.*, 18, 566

DIABETES MELLITUS

DIABETES MELLITUS

Pathogenesis

Significance of the pituitary gland

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The experiments of various investigators, particularly Young, have demonstrated that when permanent diabetes mellitus is produced in dogs by giving several injections of pituitary extract the islands of the pancreas show histological changes very like those of human diabetes mellitus. Pituitary extract contains 3 main hormones affecting carbohydrate metabolism as follows (1) glycogenic, rendering the animal insensitive to the hypoglycaemic action of insulin, (2) diabetogenic, producing rise in blood sugar, (3) pancreatrophic, giving rise to hypertrophy and hyperplasia of the cells of the islands of Langerhans. The responses obtained by the use of pituitary extract depend upon age, species and other factors. A puppy, for example, rapidly increases in growth in the first place and later on diabetes develops. There is thus established the possibilities of a relation between the growth and diabetogenic hormones.

Treatment

Insulin preparations

Barnes, Cuttle and Duncan have compared the effects of identical doses of histone zinc insulin, unmodified insulin, crystalline zinc insulin and protamine zinc insulin given under strictly controlled conditions, they found that the hypoglycaemic effects of unmodified and of crystalline insulin disappeared between 6 and 8 hours after injection, whereas the effects of histone zinc insulin persisted for from 18 to 24 hours and those of protamine zinc insulin persisted for between 24 and 36 hours. With histone zinc insulin, the action of which is more prompt than that of protamine zinc insulin, it is possible to maintain a more constantly normal blood sugar level, with absence of glycosuria, than with other preparations.

Globin zinc insulin

Globin zinc insulin is a new delayed-action insulin, containing globin insulin and a small amount of zinc, it has been in circulation in the United States of America but has not had, at the time of writing, proper clinical trial in Great Britain. If globin zinc insulin is proved superior to protamine zinc insulin the latter should be given up as a remedy since otherwise there might be confusion. Lawrence considers that there is no superiority in globin zinc insulin as compared with protamine zinc insulin. When globin zinc insulin was substituted for protamine zinc insulin in 6 hospital patients with diabetes mellitus, there was no appreciable difference in blood and urine tests. Protamine zinc insulin is weak and prolonged in action, therefore when large doses are given there is a risk of internal hypoglycaemia. On the other hand globin zinc insulin tends to control sugar by day, this is accomplished by giving a pre-breakfast dose which has the effect of preventing hypoglycaemia at night and any serious relapse before breakfast next morning. It may be that globin zinc insulin contains too much globin, it is water-clear and this in Lawrence's opinion is a serious disadvantage, because ordinary soluble insulin is also clear.

Barnes, C. A., Cuttle, T. D., and Duncan, G. G. (1941) *J. Pharmacol.*, **72**, 331.

Lawrence, R. D. (1943) *Brit. med. J.*, **2**, 103.

Young, F. G. (1941) *Brit. med. J.*, **2**, 897.

DIARRHOEA ASSOCIATED WITH FLAGELLATE INFECTION

GIARDIA INTESTINALIS

Vol IV
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Treatment

Atebrin (mepacrine hydrochloride) and quinacrine have been found useful in the treatment of giardiasis. Cade and Milhaud gave 0.1 gramme of quinacrine (a derivative of acridine) 3 times daily for the first 5 days, after which a few days' pause was observed, and then a second, third or further series followed. Stovarsol injections were also given, 0.5 gramme over 8 days, and bismuth carbonate was regularly administered in conjunction with cholagogic preparations.

Galli-Valerio also recommends 0.1 gramme 3 times a day for 5 days, with no other treatment. Many other workers, including Martin, Heilmann and Grüneis, have confirmed this. Martin also states that atebrin eradicates *Trichomonas* infections as well as *Lambia* infections, and that when given in a vaginal douche it eradicates *T. vaginalis*.

Cade, A., and Milhaud, M. (1938) *J. Méd. Lyon*, **19**, 485.

Grüneis, P. (1938) *Wien klin. Wschr.*, **51**, 605.

Heilmann, K. (1938) *Munch. med. Wschr.*, **85**, 1626.

Martin, P. (1938) *Rev. Méd. Hyg. trop.*, **30**, 32.

DIABETES MELLITUS—DIPHTHERIA DIARRHOEA IN INFANCY AND CHILDHOOD TREATMENT

Acute diarrhoea

Sulphathiazole

Cooper, Zucker and Wagoner describe the results of treatment by sulphathiazole of acute diarrhoea and dysentery in infants and children, they found that sulphathiazole was effective in cases of *Shigella paradysenteriae* infection but was not of use in other types of infection

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Cooper, M L, Zucker, R L, and Wagoner, S (1941) *J Amer med Ass*, 117, 1520

DIPHTHERIA

BACTERIOLOGY AND PATHOLOGY

Bacteriology

Distribution of diphtheria types

The use of a tellurite-containing medium has improved the bacteriological diagnosis of diphtheria, many false positive reports being eliminated. Type-determination is now generally in vogue. In 1941 the distribution of mitis, intermediate and gravis types of diphtheria bacilli, as reported by the Emergency Public Health Laboratory Service in April 1943, was analysed by examination of 8,457 swabs from diphtheria patients, these belonging to different parts of the country. The result was that Liverpool was shown to be very susceptible to diphtheria, being heavily infected with gravis strains and also responsible for about one-third of the total cases. It is interesting to compare one town with another, for example Leeds had much of the gravis and little of the intermediate strain, whereas Cardiff was small in gravis types and large in the other two. Summing up, the report said that gravis is the prevalent infective type in north-east and central England, whereas intermediate and mitis are commoner in the south-west. Even in a year there were substantial changes in the percentage of the different types in any given town or district. It is difficult to make any clear statement with regard to the mortality associated with any particular type, indeed deaths associated with the three types varied according to the place and the time. Many factors have to be considered—general, social and economic.

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Russell (W T) in analysing the factors states that the change of type may be in some way connected with the total number of susceptible children in the district: that is to say when the percentage of protected children is down the gravis type figures are up and when the degree of protection is very high the mitis type is the prevailing one. It has not been established that gravis infection means a high death rate.

CLINICAL PICTURE

Cutaneous and wound diphtheria

In the Middle East considerable trouble has been caused by the occurrence of cutaneous and wound diphtheria, presumably this is of topical importance, and likely to pass when hostilities cease. In Hurst's *Medical Diseases of War* the subject is fully discussed. Desert sore or veldt sore are typical conditions of diphtheria of the skin. Already, so far as the infection of wounds is concerned, diphtheria has shown itself clearly, in one sector nearly 11 per cent of wounds showed diphtheroids and in another 7½ per cent were similarly affected.

DIAGNOSIS

The use of the Solé or Folger-Solé swab is still favourably reported on.

Bacteriological diagnosis of diphtheria

Cooper and his co-workers have compared various media for the diagnosis of diphtheria and found that in the practical diagnosis of diphtheria the best results are given by duplicate examination, using Löffler's medium and one of the blood-tellurite-agar media. They state that when it is only possible to employ one medium a blood-tellurite-agar medium should be used, for it will give at least 10 per cent more of positive results than the Löffler medium, and is less likely to miss the most severe cases. They consider that Neill's is the best blood-tellurite-agar medium, but much experience is needed before the full value can be got out of it, and it is essential that anyone using blood-tellurite-agar media for the first time should make a careful comparison of the results obtained with these media and with Löffler's medium and should proceed to the isolation and full identification of all the strains obtained on tellurite media, until he has acquired the necessary proficiency.

TREATMENT

Prevention

Immunization

In assessing the results of Schick tests, it is no longer believed that $\frac{1}{30}$ unit of anti-toxin per cubic centimetre of blood is necessary to give a negative result, Parish and Wright found that a negative result might be given by persons whose immunity was insufficient to withstand virulent gravis or intermediate strains, a negative response

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might be given to fourfold toxin with only 0.002 to 0.0005 unit of antitoxin per cubic centimetre and to tenfold toxin with only 0.01 to 0.002 unit. As regards choice of prophylactic, present indications are that alum precipitated toxoid will be the prophylactic of the future. The preparation of concentrated antitoxin containing 6,000 or more units per cubic centimetre, obtained by pepsin digestion of the proteins, is an important advance. It is known to possess great advantages. Serum sickness after the use of these 'globulin-modified' or protein-digested antitoxins has been reduced to negligible proportions.

Russell (A.) has analysed the Scottish diphtheria immunization campaign of 1941-2. This opened at the end of November 1940, when all local authorities were supplied with toxoids A.P.T. and T.A.F. A total of 745,928 children were inoculated with a negligible number of reaction cases, the reactions took the form particularly of paralysis of arm and shoulder muscles. In all but 2 cases out of 8 children recovery was the rule. So far as post-Schick tests are concerned, the results in various places showed negative reactions varying from 90 per cent to 97 per cent.

The mortality statistics up to the end of March 1942 showed very little alteration, but it is significant that for the succeeding year (1942-3) the death rate was almost halved, in 1942 it was 2.75 per cent.

To sum up, taking Scotland as a sample of what can be done by an immunization campaign, diphtheria can be made a less serious health problem. An immunized school child is 8 times less susceptible to diphtheria than a non-immunized one and an immunized pre-school child is about 20 times less susceptible. In the event of an immunized child having diphtheria, the infection is likely to be mild and the complications few. With regard to danger of death, the non-immunized child was 100 times more likely to die than the immunized child. In England up to the end of 1942 it is calculated that there were about 5,000,000 immunized.

Standardization of A.P.T.

Of the prophylactics current in Great Britain two, alum precipitated toxoid and toxoid-antitoxin floccules, have been in general use, the former being selected for children under 10 years of age as a rule and T.A.F. for others. The standardization of potency and dosage of A.P.T. is such that it has practically displaced other prophylactics.

Enzyme digested antitoxin

Enzyme digested antitoxin is now generally used and has superseded the salt-precipitated products. It has many advantages.

Cooper, K. E., Happold, F. C., Johnstone, K. I., McLeod, J. W., Woodcock, Hester E. de C., and Zinnemann, K. S. (1940) *Lancet*, **1**, 865.

Hurst, A. (1943) *Medical Diseases of War*, London, p. 384.

Parish, J. H., and Wright, J. (1938) *Lancet*, **1**, 882.

Russell, A. (1943) *Brit. med. J.*, **2**, 52.

Russell, W. T. (1943) *Epidemiology of Diphtheria during the last Forty Years*, Medical Research Council Spec. Rep. Ser., No. 247.

DISLOCATIONS, FRACTURES, FRACTURE-DISLOCATIONS, AND ASSOCIATED INJURIES

REGIONAL

Shoulder joint

- 328 In fractures of the great tuberosity of the humerus without gross displacement, immobilization in abduction is rather liable to lead to a stiff shoulder, and it is for this type of case that relaxed circumduction from the first day gives the best results. The patient is shown how to bend over sideways with his arm hanging away from his body and, by general pendulum swinging of the arm, describe a circle with his hand, which gradually increases in circumference as pain and spasm disappear. It appears that the broken-off fragment of the great tuberosity does not become displaced by this manoeuvre, because it is performed with all the shoulder muscles relaxed, the weight of the arm being used to give the necessary distraction.

Rupture of supraspinatus tendon

- 331 A fair number of the complete tears are still missed, mainly because they are not suspected, and surgeons are rather unwilling to explore the doubtful cases. The condition is still a new entity to most of the medical profession and, as such, is worthy of emphasis. The diagnosis of complete rupture is made as follows: (1) The patient is unable to abduct the humerus to a right angle, in spite of the strongly acting deltoid. (2) When the humerus is abducted passively to the right angle the patient can hold it there, but when asked to lower it there is a click which can be felt as the head shifts from its pivoting point in the glenoid cavity and slips upward, the arm at the same time dropping suddenly to the side of the body. The patient cannot lower the arm gradually. (3) There is always tenderness over the great tuberosity of the humerus, and there is sometimes referred pain over the insertion of the deltoid. (4) Radiograms are negative.

In cases of inflammation of the supraspinatus tendon with calcification, aspiration under local anaesthesia and washing out the subdeltoid bursa with physiological saline through 2 needles give immediate relief, but may have to be repeated. The results of this treatment are quite dramatic.

Elbow joint

Internal epicondylar separations

Even when the internal epicondyle is separated and pulled into the joint, manipulation by abduction of the forearm on the arm and pull on the flexor origins may be successful in reducing it. Radiographic confirmation of reduction is necessary. In such a case the only indication for operation would be non-recovery of the bruised ulnar nerve. Pegging back or excision of the epicondyle is by no means always necessary in order to obtain a good functional result.

As regards injuries and fractures of the elbow joint, emphasis must be laid on the importance of the use of active movements only and on absolute avoidance of passively stretching the fibrous tissue, as the latter further aggravates the disability and may set up myositis ossificans.

Fractures of shafts of radius and ulna

The method described by Lambrinudi is recommended but this calls for radiographical control in the operating theatre and is mentioned as an additional argument for transfer of the patient to a fracture hospital whenever any difficulty in conservative reduction and retention is experienced.

Fractures of the lower end of the radius Colles's fracture

It is recommended that a rather longer primary plaster should be applied and that, after the period of reaction and any danger of swelling is over, the plaster should be completed with a bar of plaster or light metal to maintain the position of the wrist. This allows all sorts of active use without risk. If there is much comminution it is advisable, in order to avoid secondary collapse with shortening and distortion of the radius, to include the elbow and half the upper arm in the plaster, the elbow being at a right angle, and the radio-ulnar position being that of choice for use.

Wrist joint

Fractured scaphoid

In fractures of the scaphoid with no displacement the plaster should be applied as follows: the hand is put in radial deviation and the thumb in opposition, and the plaster should extend distally to hold the first metacarpal, the proximal half of the proximal phalanx should, therefore, be included, otherwise the distal fragment of the scaphoid is likely to have some range of movement.

Hand

Bennett's fracture

Better reduction and maintenance of position in this fracture can be achieved by a steel pin through the pulp of the thumb, and elastic traction with a piece of rubber tubing attached to an extension bow formed by strong wire incorporated in a plaster cuff round the forearm.

Mallet finger

A neat plaster splint may be made for a mallet finger by making a tube of dry plaster of Paris bandage, putting the finger into it, and pressing the finger and thumb together in such a way as to hyperextend the affected finger, then immersing the whole hand in water and moulding the plaster neatly to fit the finger. This should be left on for 6 weeks.

Pelvis

In a fracture-separation of the symphysis pubis, or other fracture in which the pelvic ring is opened up, remarkably good reduction of the fracture may be achieved by nursing the patient mainly on his sound side instead of on his back, for this position opens up the pelvic girdle.

Knee joint

The occasional incidence of a displacement of one or other of the fibro-cartilages, more commonly the external semilunar cartilage, in abduction fractures, calls for specialist treatment. This is recommended because of the difficulty of recognizing indications for open reduction of the fracture and for arthrotomy.

Fracture of the patella

Excision should still be reserved for cases with special indications such as comminuted fracture, compound fracture and failed suture. The usual transversely-fractured patella is still best treated by conventional methods.

Fractures of shafts of tibia and fibula

In non-union of fractures of the tibia the sliding bone graft fixed with vitallium metal screws has been very successful in the hands of Burns and Michaelis. Vitallium is the most satisfactory metal in use because such screws never become loosened as

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others do In making the sliding graft a graft of from 5 to 6 inches in length is cut in the bone above the level of the fracture and half that length of bone is removed from the subcutaneous surface below the fracture Since the graft is slightly tapered from above downwards it can be slid down until it forms a bridge between the two fragments If the fracture is near the upper end of the tibia it may be necessary to slide the graft from below upwards When the graft has been fitted it is fixed by the insertion of from 4 to 6 vitallium screws The Sherman pattern is best, the bone being drilled and the screws fixed in the usual way The limb is then put up in well padded plaster applied from the groin to the toes After a fortnight the plaster is removed, the stitches are taken out and a lightly padded walking plaster is applied The patient may be allowed to walk 3 weeks after the operation The results of the above treatment are satisfactory and by using the method described there is no need to borrow bone from the unaffected tibia

Complications of spinal fractures

Paraplegia

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Interference with bladder function always involves a decision whether the bladder should be drained suprapubically, by tied-in catheter, or by repeated catheterization The bladder receives sympathetic supply from the first and second lumbar cord segments, this relaxes the detrusor and closes the sphincter The parasympathetic supply from the second and third sacral segments causes contraction of the detrusor and relaxation of the sphincter If, therefore, the lesion of the cord is above the first segment, it is reasonable to expect a traumatic local cord reflex emptying the bladder after a few weeks In these cases one can temporize with manual expression or intermittent catheterization Should the fracture be at the sacral segment of the cord, that is the first lumbar vertebra, then the parasympathetic innervation is damaged and automatic bladder function cannot develop because the sympathetic is unopposed In these cases early suprapubic drainage should be instituted and the bladder irrigated from the urethra and out through the suprapubic tube Prolonged use of a tied-in urethral catheter has drawbacks in that it often sets up urethritis with ascending complications Intermittent catheterization with all aseptic precautions, including handling the catheter with dissecting forceps only, is safe in these cases even for a prolonged period

Burns, B H, and Michaelis, L S (1944) *Lancet*, 1, 337

Lambrinudi, C (1940) *Proc R Soc Med*, 33, 153

DIVERTICULOSIS AND DIVERTICULITIS

Addenda

In section on *The stage of established diverticulosis*, paragraph on Symptoms, Vol IV, p 211, last line, after 'defaecation' add the following 'or persistent desire after voiding'

In paragraph on *Aperients*, p 215, last line, after 'enough' add the following 'Dose first thing in the morning on getting out of bed, or plain Petrolagar, that is without phenolphthalein or cascara, may be used'

In paragraph on *Colonic douches*, p 217, after the fourth sentence add the following 'We find that olive or other digestible oil is less well tolerated over a period than liquid paraffin'

In paragraph on *Enemas and dugs*, p 217, after the first sentence add the following 'The saline should be fairly warm, about 100° F'

Corrigendum

In section on *Treatment* (1), p 215, 1 2 should read 'a normal appearance by treatment with hot saline douching (temperature about 100° F)'

INTRODUCTION AND DEFINITION

Stomach diverticula

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Reich found a gastric pouch in 6 cases out of 19,022 X-ray examinations, that is in 0.03 per cent He describes the 6 cases, and 2 others from private practice, with clinical, X-ray and gastroscopic details In more than half the recorded cases there are not any symptoms In the others the order of symptoms is (1) pain, (2) belching, (3) mild to moderate epigastric tenderness, (4) dysphagia, relieved by oesophageal dilatation, (5) abdominal distension, other causes being excluded, (6) bleeding, this may occur in children Excision is advised by the author, if it is established that the disturbances arise from the pouch

STAGES

The stage of established diverticulosis

Duodenum and jejunum

Acquired diverticula are often multiple and commonly arise from both sides of the intestine near the mesenteric attachment alongside the vessels, they are compared by Bunch to the tracking of an epigastric hernia along the artery through the fascia Probably neither develops until muscular tone is beginning to be lost

Wigand found 21 such pouches in 7,295 necropsies, that is 29 per cent of all bodies

Diverticulitis

Diverticulitis is not uncommon in women, and Wetherell remarks that it may resemble in all its manifestations pelvic inflammation with in addition the symptoms of low intestinal obstruction. The uterus may be tender, the bladder involved and the tumour sometimes on the right side, walking or jarring, defaecation and micturition cause pain.

The X-ray appearance of a chronic perforation into the mesentery, illustrated in Plate IX, Vol IV, facing p 216, is described by Ledoux-Lebard as the cauliflower appearance.

Complications

Vesico-intestinal fistula

The cause of vesico-intestinal fistula is inflammatory lesions of the bowel in just over one-half of the cases, and of the inflammatory lesions diverticulitis is a primary cause in two-thirds of the cases. Other causes may be tumour and carcinoma of the rectum. The warning signals are urological symptoms, increased urination, mild burning and constant or intermittent pyuria. Gas and faecal matter in the urine or urine in the stool are signs of an actual fistula but the fistula may exist without these signs. Observation may be made by using a solution of indigo-carmin which is put into the bladder and its discharge watched as it comes through a rectal tube, the proctoscope may also be used. The diagnosis is sometimes made by the use of a barium enema. On cystoscopic examination of a fistula between the colon and the bladder a small area of redness is seen in the early stages. Diagnosis, therefore, at an early stage depends upon the cystoscope. So far as treatment is concerned there is a sequence of operations. The first procedure is to put in an indwelling urethral catheter, now and then suprapubic cystotomy may be carried out. Sulphonamides given by the mouth and applied locally at operation are of great value.

Enterocolic fistula

Shallow describes this as one of the most serious complications. If the perforation is into the upper part of the small intestine many feet may be side-tracked. The local inflammation may subside but anaemia and emaciation follow and extensive resection may be needed. If possible an end-to-end union of the small intestine should be made.

DIAGNOSIS OF DIVERTICULITIS

Krogdahl shows how closely a diverticulitis can resemble carcinoma radiologically if a barium enema only is given. According to Schatzki the diagnosis is easy in most, difficult in some and impossible in a few. At operation it is often not clear, even when the specimen is examined macroscopically. Good preliminary radiological examination, when the condition of the patient allows, is more accurate. The palsade or accordion appearance of diverticulitis (shown in Vol IV, Plate V, p 212, and Plate VII, p 214) and the bizarre fringed contour which develops later indicate diverticulitis, and some pouches can usually, although not invariably, be seen near by. These do not, however, exclude cancer, they make the diagnosis of diverticulitis more probable but they may be incidental, and their absence is more helpful than their presence. In a cancerous area the mucosal relief picture is usually absent. Case warns against over-distension with air, stating that he has twice seen rupture of the sigmoid. In the presence of obstruction he advises caecostomy for immediate relief and diagnostic examination with a barium enema a week or two later. Caecostomy is the correct preliminary treatment in either case. Feldmann mentions that a change in the size of the tumour on palpation is in favour of diverticulitis. How diverticulitis may develop with few signs is perhaps shown by Wigand's record that of 22 cases of diverticulitis found at necropsy symptoms had been observed in 6 only, and the diagnosis made in one. Death was due to the diverticulitis in 5 of the cases.

Sigmoidoscopic examination, in the experience of Shipley and Gerwig, and of Spriggs, is diagnostic in a few cases and very often negative. It is most helpful to differentiate between carcinoma and diverticulitis, when the lesion can be reached, and to ascertain the length of healthy mucous membrane below any lesion. Buie (see also Jackman and Pumphrey) describes accessory signs in the sigmoid. A sacculation of the sigmoid, which he confirmed by X-ray examination, consists of shallow larger pouches with ridge-like elevations between. This was seen in 3 cases from one to 6 years before diverticula were demonstrated. Other signs are immobility of the gut, and sharp angulation or narrowing with increase of folds or mucosal oedema, so that the instrument cannot be passed the usual distance. These signs may be due to other causes of pelvic inflammation and are presumptive evidence only. Spriggs confirms the value of observing angulation and narrowing. Any inflammatory sign is unusual on the distal side of a diverticulitic contraction.

Of diverticulitis

Laufman, from the review of 5 series of reported cases, gives the surgical mortality for diverticulitis of the colon and its complications as from 10 to 18 per cent. For radical operations, mostly resections, it appears to have been from 18 to 23 per cent. He concludes that the trend is, as above implied, towards conservative management.

- Buie, L. A. (1939) *New Engl J Med*, **221**, 593
Bunch, G. H. (1939) *Sth med J*, **32**, 919
Case, J. T. (1940) *Radiology*, **34**, 651
Feldmann, M. (1940) *Radiology*, **34**, 651
Jackman, R. J., and Pumphrey, R. E. (1939) *Proc Mayo Clin*, **14**, 596
Krogh, T. (1939) *Acta Radiol, Stockh*, **20**, 241
Laufman, H. (1941) *Surg Gynec Obstet*, Section International Abstract of Surgery, **73**, 222
Ledoux-Lebard, G. (1937) *Medecine*, **18**, 538
Reich, N. E. (1941) *Amer J digest Dis*, **8**, 70
Schatzki, R. (1940) *Radiology*, **34**, 651
Shallow, T. A. (1940) *Penn med J*, **43**, 1443
Shipley, A. M., and Gerwig, W. H., Jun. (1939) *Surg Gynec Obstet*, **69**, 474
Spriggs, E. I. (1938) *Quart J Med*, **31**, 588
Wetherell, F. S. (1938) *Amer J Obstet Gynaec*, **35**, 417
Wigand, H. (1940) *Beitr path Anat*, **104**, 38

DROPSY, EPIDEMIC

AETIOLOGY AND PATHOGENY

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The pathogenesis of epidemic dropsy is still obscure. Observations on the subject, especially on the basis of necropsy findings, are few, but from them it is apparent that the striking abnormality, uniformly noted, is principally a vascular phenomenon, namely dilatation of the capillaries and extreme engorgement. There has been a good deal of speculation on the cause of such phenomena, but nothing definite has so far been established.

Hypotheses of causation

Beri-beri hypothesis

It is now definitely settled that epidemic dropsy has nothing to do with beri-beri, and no evidence has been adduced in favour of its being a vitamin deficiency disease.

Mustard oil hypothesis

Kamath described an outbreak of epidemic dropsy in an area where mustard oil was not consumed, in which oil expressed from 'odissimari' seeds was implicated, these seeds were found to be identical with *Argemone mexicana* seeds. The epidemiologically implicated mustard oils almost always gave a positive nitric acid test for argemone oil (Stewart and Boyd, Lewkowitsch).

It is most probable that the substance responsible for the reaction with nitric acid is not associated with the causation of epidemic dropsy. At present it cannot be certainly concluded that epidemic dropsy and argemone oil poisoning are identical. It is also not definitely decided whether or not any other vegetable poison can produce the same symptoms.

MORBID ANATOMY

Extensive studies have been made in recent years on the chemical and cytological changes in the blood in epidemic dropsy. Chopra and his colleagues found that in the serums of patients both relative viscosity and surface tension are below their normal values. The total nitrogen, and consequently the protein values, was found by Roy to be much below the normal although the serum protein was about the normal in most cases. In acute cases the cholesterol content is within the range for normal Indians but the average is somewhat higher. In chronic and recurrent cases there is a marked increase of the cholesterol content. The average lipid-phosphorus figures show normal values in both acute and chronic cases. It is suggested that the increased cholesterol values may be a compensatory mechanism to increase the colloid-osmotic pressure of the blood which is markedly lowered in epidemic dropsy.

- Chopra, R. N., Mazumdar, D. C., and Roy, A. C. (1940) *Indian J med Res*, **27**, 937
— Pasricha, C. L., Goyal, R. K., Lal, S., and Sen, A. K. (1939) *Indian med Gaz*, **74**, 193
Kamath, A. V. (1928) *Indian med Gaz*, **63**, 555
Lewkowitsch, J., and Warburton, G. H. (1922) *Chemical Technology and Analysis of Oils, Fats and Waxes*, p. 143
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DROPSY, EPIDEMIC—DRUG ADDICTION

DROWNING RESUSCITATION

DROWNING

Banting and his colleagues describe two types of drowning. In type I there is apnoea with an initial struggle, followed by cessation of movement and swallowing, leading to gastric distension. This is followed by vomiting and gasping, when water may be heard to enter the lungs. Somatic activity then ceases. In this type the blood pressure falls suddenly just before death, the heart rate decreases, fibrillation often occurs, and electrocardiographic activity ceases within 1 or 2 minutes. In type II the initial apnoea continues, and is not followed by gasping, very little water entering the lungs. The blood pressure falls more gradually, the heart rate decreases by 10 to 15 beats per minute, and after a time the ventricular complexes of the electrocardiogram cease, the auricular complexes may, however, persist for from 30 to 45 minutes. These experiments indicate the extreme importance of laryngeal spasm. The authors considered the slow heart rate to be due to vagal influences. Blood-gas analysis showed that the oxygen decreased rapidly to from 2 to 3 volumes per cent and that the carbon dioxide also, after an initial rise, fell, this confirms the contention of Yandell Henderson.

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RESUSCITATION

General survey

On the basis of their experimental work Banting and his co-workers recommend, in addition to the usual measures, that the larynx should be swabbed with a 10 per cent solution of cocaine hydrochloride, and a catheter be passed into the trachea, if there is evidence of laryngeal spasm as suggested by difficulty in securing a free airway. They also found insufflation of amyl nitrite to be helpful in type II drowning, and emphasize the value of full doses of atropine sulphate ($\frac{1}{30}$ to $\frac{1}{15}$ grain) in combating vagal inhibition, and of adrenaline hydrochloride in large doses (40 minims of a 1 in 1,000 solution). They stress the importance of early and prolonged artificial respiration, urging that it should be continued until rigor mortis sets in.

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Artificial respiration

A 3-year survey is being carried out in the United States of America in which both manual and mechanical methods are being subjected to a prolonged test. So far there has been a total of over 2,000 cases, chiefly drawn from the United States coast-guards, who use the Howard-Sylvester method, and the fire departments of Los Angeles and Chicago, which employ mechanical devices, among the latter are the E and J resuscitator, the E and J inhalator and the H and H inhalator. Neither the method of Schafer nor that in which mechanical devices are used caused any injury. In all cardiac cases the outlook is bad. Unless treatment is begun within 15 minutes of stoppage of breathing a fatal result is to be looked for.

Banting, F. G., Hall, G. E., Janes, J. M., Liebel, B., and Loughheed,
D. W. (1938) *Canad. med. Ass. J.*, **39**, 226.

DRUG ADDICTION

AETIOLOGY

A rather rough but suggestive and useful classification of addicts has been given by Neuberger. He divided morphine addicts into (1) morphinomaniacs or true addicts and (2) morphinists.

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Psychopathic origin

Morphinomaniacs are those who resort to the drug in virtue of a kind of predestination due to a defect in their psychical make-up. Clinically they answer to the designation of *petits melancoliques*; they must have a stimulus from the outside, being incapable of providing it from their own resources. They use the drug to provoke 'a momentary suicide'. Cure of these subjects is particularly arduous and they usually relapse.

Secondary or exciting causes

On the other hand, in morphinists the habit is not accompanied by a deep-seated need for the poison. Their psychical make-up may not deviate greatly from the normal, and their habit is often due to suffering, that is as a sequel to some painful affection, for which the usual analgesics have proved useless. Often the drug has been brought to their notice by their medical attendant or an associate.

CLINICAL PICTURE

Addiction properties of opium derivatives

The League of Nations has collected in a Bulletin, from various sources, what is perhaps the most comprehensive summary available of the properties of some of the more modern drugs derived, directly or indirectly, from opium. Particular reference is made to eukodal, dicodid, dilaudid, and acedicone.

As in the case of heroin it was thought at first that these newer drugs were either devoid of the habit-forming properties of morphine or that the risk of habit formation was so slight as to be almost negligible.

A mass of experimental and clinical evidence, however, is now available which conclusively shows that all the above-mentioned drugs are, with improper usage, liable to give rise to addiction. There are, however, variations in this liability. The danger would appear to be least in the case of dicodid, and dicodism seems to be more readily curable than addiction resulting from other members of this group and the abstinence symptoms milder. When addiction is due to acedicone (acetyldihydrocodemone), this may take a severe form with marked abstinence symptoms. In respect of eukodal (dihydrohydroxycodemone), both the symptoms of the addiction state and the abstinence syndrome would not appear to differ greatly from those of morphinism. It must, however, be admitted that primary eukodal addiction is rare. Most of the reported cases are secondary, the eukodal having replaced morphine.

The opium smoking habit

Chopra and Chopra^{1, 2} stress the importance of example, one smoker makes many, and heredity plays little or no part. The addicts are mostly young when the habit is first contracted (10 to 30 years old). It is interesting to note that, in the authors' series, no less than 50 per cent smoked entirely for the euphoric effects attained. These were mostly young persons corrupted by association with other smokers. Next most common, and least blameworthy of the exciting causes, was a desire to obtain relief from suffering induced by disease—especially diseases of the respiratory system. This accounted for 33.3 per cent of the cases. Also, more or less excusable, was indulgence in the habit to mitigate the stress and strain of hard work and to combat fatigue, 13.3 per cent gave this as the cause.

Hemp addiction

As pointed out by Adams, the German traveller Engelbert Kaempfer, in his *Amoenitates Exoticae*, was the first to show that the innocuous European hemp was the same plant as the Asian variety modified by soil and climate. Hemp becomes Indian hemp in India, marihuana in America and Mexico, and dagga in South Africa. All are varieties of *Cannabis sativa*. Much has been written recently on hemp addiction. The habit in India has been reviewed by Chopra and Chopra³. Dagga smoking in South Africa has been investigated by the staff of the Pretoria Mental Hospital (Report), the abuse of marihuana in the U.S.A. has been described by Yawger, and Fontoynt has reported on hemp intoxication in Madagascar.

Both the Chopras and Yawger make some interesting observations on the relation of hemp addiction to crime. Both agree that alcohol is a more potent agent than hemp in crime production. The Chopras go so far as to say that, as regards premeditated crime, especially of the violent kind, the hemp drugs may actually serve as deterrents owing to their quietening and stupefying effects. Yawger, however, claims that hemp (marihuana) uncovers any antisocial or sadistic elements in the personality rather than directly incites to crime. Fontoynt remarks that, among the good-natured Madagascans, hemp may give rise to a state of aggressive excitement which, however, rarely progresses to homicidal mania but results in public fights and brawls. The habitué may become tiresome, pugnacious and unjust.

The coca habit

Wolff wrote an interesting paper upon coca chewing in South America. This habit he prefers to term 'cocaism' in contra-distinction to 'cocainism' which is, for obvious reasons, much more serious. The mastication of coca leaves is especially prevalent in Peru and Bolivia and, although to a lesser extent, in North Argentina. It is met with principally among the poorer inhabitants of the mountain districts, especially among the aboriginal Indians, also among the peoples of the Sierras and higher plateaux, among persons who undergo hard labour in the mines and in agricultural labourers. The total number of chewers has been estimated at between six and seven millions. The habit is frequently associated with alcoholism. It begins in childhood and lasts for life. Among the habitues misery is rife, and poverty, insanitary surroundings, malnutrition and epidemics, including syphilis, are the common lot. It is still a moot point, however, whether coca chewing is responsible for the above conditions or whether bad conditions lead to the resort to coca.

Even experienced physicians are not agreed whether the habit *per se* is really harmful or not. Some regard it as actually being beneficial, in high altitudes especially, others are of opinion that its suppression would eliminate 90 per cent of the ills of the men in the Sierras. One physician even suggests that the ill success of the Bolivians in their struggle with the Paraguayans might have been due to the fact that the Bolivian soldiers were liberally supplied with coca whereas their adversaries were not. Wolff, who has resided in the Argentine for some time, pleads for a dispassionate and scientific investigation of the problem, and points out that such an inquiry has not hitherto been made. The difficulties in the way are, he admits, great. The habit is encouraged by certain employers who are out to exploit the Indians. Coca chewing blunts the faculties, renders its victims docile and more or less impervious to their surroundings and, moreover, the leaves are often accepted in lieu of an adequate wage. Whatever may be the harm which is done or is not done by cocaism, it seems

to be established that its concomitants are often poverty, malnutrition, insanitary conditions and exploitation

TREATMENT

Stungo emphasizes the desirability of certain alterations in the law which would give the physician more control over the voluntary patient, and would afford the legal offender the opportunity of undergoing treatment without the stigma of imprisonment. On the first count, he advocates the signing of a declaration by the patient, similar in form (but with suitable modifications) to that which is in use for voluntary treatment under the Mental Treatment Act 1930. Compulsory notification is also urged to render more difficult the patient's approach to more than one doctor. The procedure suggested is immediate notification of the Home Office by telephone, followed by filling in of a prescribed form. 'Cures' should also be notified, with the object of focusing attention on the relapsing addict. On the second count, the reform he urges is that, in cases of offences against the Dangerous Drugs Act, the offender should be offered—as an alternative to imprisonment—discharge to the care of a medical authority. Failure to complete the cure would render the patient liable to imprisonment under the original charge. He also suggests that such treatment might be under the jurisdiction of a body with functions similar to those of the Board of Control.

Curative

Special withdrawal methods

The results of some valuable researches into the efficacy of various withdrawal methods have been published in the United States, where material is abundant. Especially important is a paper by Kolb and Himmelsbach, who attributed the divergent statements made about the worth of any given treatment mainly to the following factors: (1) absence of a proper system of controls, (2) unsuitable clinical material, and (3) failure to realize that addicts with the same degree of physical habit reacted to the discomfort of withdrawal with widely different degrees of mental intensity. As regards (2) it was pointed out that about 80 per cent of the addicts at the present day have such mild habits that they are useless for testing the value of treatments. To obviate the difficulty mentioned under (3) they have devised 'a simple, impersonal, and quantitative method for estimating the intensity of the abstinence syndrome'. This ingenious method is based upon a system of assessing 'points' both for certain accurately measurable signs, such as rectal temperature, respiratory rate, basal metabolic rate, and blood pressure, and for the presence and intensity of non-accurately measurable signs, such as yawning, lacrimation, perspiration, anaemia, tremor and restlessness.

The barbiturates—Stungo has a high opinion of the value of the barbiturates, especially soluble hexobarbitone and its congeners, when they are carefully administered. Not only are they efficacious in relieving the withdrawal symptoms but he has also found that they can be manipulated as 'truth drugs' whereby it is made more difficult for the patient to deceive his doctor. When given cautiously and in as low a dose as possible for effectiveness they do not markedly affect the speech and hearing, but produce a certain clouding of consciousness which hinders the patient from appreciating all the implications of a question and from framing a plausible lie. Advantage may also be taken of the cerebral blunting to question the patient about the origin of his addiction and to explore the circumstances which touched off the neurosis of which the addiction is a symptom. It is, of course, assumed that the patient can be placed in a nursing home or suitable institution.

As regards psychological treatment, the author points out that in 'accidental' addiction, that is after painful illness or operation (Neuberger's 'morphinist' type, *vide supra*), the superficial forms of psychotherapy will suffice. In the psychopathic form of addiction ('morphinomaniacs') deep exploration is necessary.

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Bull. Hlth Organization L. O. N. (1939) 8, 387.

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— (1938) *ibid.*, 73, 81, 132, 193.

— (1939) *Indian med. Res. Mem.*, Suppl. Series to *Indian J. med. Res.* 1939, July, Memoir No. 31.

Fontoynt, M. (1938) *Bull. Soc. Path. exot.*, 31, 446.

Kolb, L., and Himmelsbach, C. K. (1938) *Publ. Hlth Rep. Wash.*, Suppl. No. 128.

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Report of an Investigation by Medical Staff, Pretoria Mental Hospital (1938) *S. Afr. med. J.*, 12, 71, 85.

Stungo, E. (1941) *Brit. J. Inebri.*, 39, 37.

Wolff, P. J. O. (1940) *Schweiz. med. Wschr.*, 70, 606.

Yawger, N. S. (1938) *Amer. J. med. Sci.*, 195, 351.

DRUG ERUPTIONS

COMMON DRUG ERUPTIONS

Barbiturates

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Many types of erythematous, eczematous, urticarial, bullous and, more rarely, fixed eruptions have been reported. Cases of exfoliative dermatitis have been described, one with a fatal outcome and another with a photo-sensitization dermatitis arising 3 months after the first eruption, even after this interval barbitol was found in the urine. The retention of a drug and its subsequent delayed excretion may be the explanation of toxic eruptions of obscure origin and, when reliable tests for a suspected drug are available, the urine should be examined.

In a paper on 'Exfoliative Dermatitis due to Phenobarbital' Winer and Baer review the literature on visceral lesions in cases of drug eruptions and give a clinical and very detailed report on the necropsy in a case occurring in a woman, aged 47 years. Macroscopical and microscopical observations showed diffuse acute inflammatory reactions in all the organs and tissues which were examined, and are a timely reminder that the toxic effects of a drug are very unlikely to be limited to the skin.

Bismuth

This drug, like mercury and gold, may be deposited in the skin or mucous membranes, and a case of carcinoma of the cervix has been described in which bismuth therapy produced an apparent vaginal melanosis of marked degree.

Codeine

Hypersensitivity to codeine was reported first in 1893. The lesion was described as being formed by papules, the size of a pin-head, on a red base, the reaction occurred on the face and on the upper part of the thorax. Other cases have been described since, characterized chiefly by erythematous rash appearing on the arms, trunk, abdomen and the inner sides of the thighs and knees. In all cases the eruptions quickly disappeared after codeine administration ceased. Altogether 10 cases have been described, the last by Seidmann, who gave details of a case of generalized erythema caused by the taking of 3 codeine phosphate pills of 0.015 gramme each. The rash appeared a few hours later. There was an eosinophilia of 15 per cent.

Gold

Two cases of 'pityriasis rosea-like dermatitis following gold therapy' are reported by Wile and Courville. Similar eruptions have been described before and, although some of them closely resemble pityriasis rosea and run the brief course of that disease and are probably provoked by or are merely coincident with gold therapy, it seems certain that an eruption due to gold may take the pattern of pityriasis rosea. Suggestive of its drug origin are the deeper colour tones of purple or brown, the persistence of the lesions after 2 months and the marked residual pigmentation. The latter is interesting in view of the permanent pigmentation which may affect the exposed skin after parenteral injections of a gold preparation, and Schmidt defines this condition by the term chrysiasis. Since treatment for chrysiasis is unsatisfactory he advises limiting the total dosage to 50 milligrams of gold sodium thiosulphate per kilogram of body weight, avoiding undue exposure to ultra-violet light and inadvertent paravenous injections.

Iodides

That bullous iodide eruptions are particularly liable to occur in subjects of cardiac and renal disease has long been known. Adamson reported 3 more cases of iodide eruptions in patients with bacterial endocarditis and renal disease from St Bartholomew's Hospital, London, all of these were fatal. In one patient the eruption appeared after the administration of a total of 90 grains of potassium iodide. The second was a man aged 34 years, in whom blisters developed after 7 doses each of 5 grains of potassium iodide. In the third patient, aged 40 years, the eruption appeared after one dose of 5 grains of potassium iodide, and showed that defective elimination cannot be the main factor in causation, as only 5 grains of potassium iodide had been ingested.

Sulphanilamide

Sulphanilamide has been responsible for various eruptions, erythematous or urticarial, in macules, papules or larger lesions and even exfoliative dermatitis. Since the drug may induce sensitization of the skin to light, some eruptions are due to a combination of both factors.

Wien and Lieberthal report a fatal case of a pemphigus foliaceus-like eruption supervening on acute otitis media and mastoiditis in which the patient was treated by sulphanilamide. A general morbilliform eruption marked the end of sulphanilamide therapy and the eruption had almost gone in 3 days, the morphology and clinical course indicating a drug rash. About 3 weeks later a generalized malodorous dermatitis developed and, after almost resolving with residual pigmentation in about 6 weeks, bullae shortly appeared and the disease ran a course fairly characteristic

DRUG ERUPTIONS—DYSENTERY, BACILLARY

of pemphigus, even to its fatal issue. It is very improbable that this was a true drug eruption.

Sulphanilamide must be added to the list of drugs causing fixed eruptions, since Goodman and Arthur report a case in which skin lesions of an unusual pattern recurred in the original sites after a test dose of sulphanilamide, although sulphapyridine did not have any provocative effect upon the fading eruption.

T A B vaccine

Van Rooyen, Rhodes and Ewing review the striking incidence of herpes labialis after a provocative dose of T A B in patients with gonorrhoea who were treated by full doses of sulphapyridine, and they conclude that this drug greatly enhanced the herpetogenic effect of the T A B vaccine. In such instances it is clear that herpes is not a true drug eruption but is evidence of the activation of a latent infection.

Adamson, H. G. (1938) *Brit J Derm*, **50**, 167

Goodman, M. H., and Arthur, R. D. (1941) *Arch Derm Syph*, N Y, **43**, 692

van Rooyen, C. E., Rhodes, A. J., and Ewing, A. C. (1941) *Brit med J*, **2**, 298

Schmidt, O. E. L. (1941) *Arch Derm Syph*, N Y, **44**, 446

Seidmann, M. (1943) *Arch Derm Syph*, N Y, **47**, 654

Wien, M. S., and Lieberthal, E. P. (1941) *J Amer med Ass*, **117**, 850

Wile, U. J., and Courville, C. J. (1940) *Arch Derm Syph*, N Y, **42**, 1105

Winer, N. J., and Baer, R. L. (1941) *Arch Derm Syph*, N Y, **43**, 473

DWARFISM AND INFANTILISM

CLINICAL PICTURE

Dwarfism combined with infantilism

Endocrine infantilism

Renal dwarfism with diabetes insipidus—Diabetes insipidus may be found associated with renal dwarfism. The main signs are dwarfism, disordered kidney function with albuminuria, diabetes insipidus and the usual signs of infantilism. Thirst is a prominent symptom, in one case there was a craving for lemons. The hereditary factor is strong. A case was described by Moehlig in which a boy of 5½ years was affected as described above. In a condition of extensive hydrocephalus the child had a primary defect of the pituitary gland, the latter confirmed by X-ray examination. Hormone treatment is of doubtful value, it may do more harm than good. The prognosis is bad.

Moehlig, R. C. (1943) *Amer J Roentgenol*, **50**, 582

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DYSENTERY, BACILLARY

BACTERIOLOGY OF THE DYSENTERY GROUP OF BACILLI

The mannitol-fermenting group

The *Bacillus dysenteriae* Sonne subgroup which produces acid in lactose and saccharose after some days of incubation remains unchanged. *B. dysenteriae* Sonne is the only member known to be pathogenic; other organisms giving these biochemical reactions, but of different antigenic structure, are not uncommonly isolated from normal stools.

The *B. dysenteriae* Flexner subgroup has now been clearly defined. It has been shown that the organisms previously included in this subgroup possess a common group antigen, and that each valid type has an individual type antigen. Accepting the possession of this group antigen as the essential characteristic of the Flexner subgroup, 2 further types, identified in India, and now found in various parts of the world, have been included. Further, the so-called Newcastle bacillus is for the same reason included, despite its anomalous biochemical reactions. This is justified by the fact that its antigen (type specific plus Flexner-group) is common to several strains, one being identical with classical Flexner, another being the commonest member of the so-called *alkalescens* subgroup, and a third being the Manchester bacillus which produces acid and gas in glucose, mannitol and dulcitol. It is considered that the strain giving true Flexner biochemical reactions is the original type, and that the others are 'biochemical' variants. It is proposed, when investigations are complete, to allot numbers to the various types in this Flexner subgroup. A number of unclassified types remain which have the biochemical reactions of the Flexner subgroup but which do not possess its group antigen. These, together with certain late fermenters of dulcitol, previously included in the *alkalescens* subgroup, may be placed for the present in a loose subgroup. There is conclusive evidence that certain of these types cause bacillary dysentery. So far (with one unpublished exception) they have not been reported outside India.

Further work in India confirms previous observations made on organisms of this group. Despite careful investigation, there is nothing to suggest that any important

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types have been overlooked, either in the subgroup which produces acid in lactose or saccharose after some days' incubation, or in the Flexner subgroup

It was suggested in 1940 that the so-called Flexner subgroup should be regarded as containing two types, the first embodying those races which are endowed with the group antigen common to the Flexner organisms, the second comprising other pathogenic races which have similar biochemical reactions but are devoid of Flexner group antigen For the first type the name *B dysenteriae* Flexner is retained, for the second, the name *B dysenteriae* Boyd has been suggested The proposed nomenclature is shown in the accompanying Table

NEW NAME		OLD NAME	
<i>B dysenteriae</i> Flexner	I	Andrewes and Inman	V
"	II	"	W
"	III	"	Z
"	IV	Type 103	
"	V	P119	
"	VI	88-Newcastle-Manchester group	
<i>B dysenteriae</i> Boyd	I	Type 170	
"	II	P288	
"	III	D1	

It will be observed that Andrewes's X and Y races have been omitted This is because they are believed to be variants and not valid types

TREATMENT

General treatment

Chemotherapy

Sulphaguanidine — Sulphaguanidine continues to give excellent results in the treatment of acute and chronic bacillary dysentery The dose recommended remains much the same When the drug is administered even in large doses a blood concentration higher than 3.5 milligrams per cent of free sulphaguanidine is rarely produced Unexpectedly high concentrations in the urine have been found in a few cases tested in the Middle East There have not been, however, any urinary or other toxic manifestations observed to result from the administration of even large doses of the drug

Trials of other sulphonamide derivatives suggest that, provided they can be given in sufficiently large doses without producing toxic effects, equally good results in the treatment of bacillary dysentery can be expected

A preliminary report on the treatment of some hundred cases of proved Shiga infections with sulphaguanidine has recently been received from the Middle East The detailed information includes full laboratory and sigmoidoscopic observations In view of the fact that the cases which were selected for the report were all of intense infections exhibiting severe symptoms, the investigation represents an exacting trial of the value of the drug in bacillary dysentery In acute cases the average dose of the drug administered was 20 grammes per day, with an aggregate of some 140 grammes in each case A high blood concentration was aimed at during the early stages of treatment

Clinically, improvement in the patient's general condition can be expected within from 24 to 48 hours after beginning treatment, the patient experiences a feeling of well-being, the abdominal pains and tenesmus are lessened and the fever rapidly subsides, reaching normal within from one to 3 days A rapid improvement in the motions also takes place, blood disappearing from the faeces and the number of stools diminishing to one or two daily within from 5 to 6 days The earlier the treatment is commenced the more rapid is the response but even in chronic cases the results have been most promising, 75 per cent showing complete healing of the colon Experience in the use of the drug is as yet insufficient for the optimum dosage to be stated but it is at present recommended that the initial dose should be about 0.1 gramme per kilogram of body weight and the maintenance dose should be 0.05 gramme per kilogram of body weight every 4 hours until the number of stools is reduced to 5 or less in the 24 hours, when the interval between the maintenance doses should be increased to 8 hours, this dosage is continued for 3 days In no case should the drug be administered for a period of more than 14 days In most cases it has been possible to stop specific treatment in a much shorter time As in the case of other sulphonamide drugs, the fluid and saline intake should be adequate and it is desirable to maintain an ample flow of urine

Hopeful results have also been obtained from attempts to free the bowel from dysentery organisms in so-called bacillary dysentery carriers by a course of sulphaguanidine treatment

Succinylsulphathiazole — Various trials have been made of succinylsulphathiazole (sulphasuxidine) The action of this drug is such that sulphathiazole is set free in the intestine The dose generally recommended varies from 0.2 gramme to 1 gramme per kilogram of body weight The treatment may be expected to last for from 4 to 17

days Succinylsulphathiazole is reported as giving results quite as good as those obtained by sulphaguanidine medication

Review of modern treatment

Manson-Bahr sums up the modern treatment of bacillary dysentery by saying that in acute bacillary dysentery large initial doses of sodium sulphate should be given. So far as diet is concerned, arrowroot may be plentifully supplied but milk should be restricted, about from 4 to 6 pints of fluids should be taken by the patient every day and a little brandy may be added. In severe cases blood transfusion is indicated. Antidysenteric serum should be administered intravenously only when there is a severe Shiga infection and 80 cubic centimetres should be given as early as possible. In chronic bacillary dysentery eusol is effective when given by colonic irrigation. In some cases caecostomy is required. As mentioned above, sulphaguanidine is most effective in acute and chronic cases, from 6 to 9 grammes being given daily for 5 days.

Therapeutic serums and vaccines

Antitoxin

Recently a specially refined antitoxin has been employed successfully in the treatment of Shiga infections. This product contains 100,000 units of Shiga antitoxin in 5-7 cubic centimetre quantities. Reports on the effects of intravenous administration of this concentrated antitoxin in doses of from 50,000 to 100,000 units in the treatment of fulminating toxic cases continue to be very favourable. This type of antitoxin is purified by means of proteolytic enzymes. It causes practically no serum reaction and appears to be the most promising of all the Shiga antitoxins tested.

Manson-Bahr, P. H. (1942) *Brit med J*, 2, 346, 374

DYSMENORRHOEA

AETIOLOGY

Basic causes

According to Randall and Odell there are two basic factors in primary dysmenorrhoea, these being first the state of ovulation and secondly the existence of a nulliparous cervix, the associated uterine distension gives rise to contractions which cause the typical cramping pain.

Investigation with intra-uterine balloon

Advances in the knowledge of the causation of dysmenorrhoea have been made as a result of Bickers's investigations with a kymograph and intra-uterine balloon. It is established that normally the uterine contractions in the follicular phase are of low amplitude and considerable frequency and associated with uterine tonus, whereas during the pre-menstrual and menstrual phases the contractions are of higher amplitude, less frequency and with lesser tonus. Tracings taken from patients with dysmenorrhoea and during the occurrence of menstruation show the uterine tonus to be greater than that it is in the pre-menstrual phase. Biopsy of the endometrium proved that these patients were undergoing typical progesterone changes. It is thus obvious that an increased uterine tonus is the one definite uterine abnormality which was proved to exist in young women of an average age of 21 years who suffered from painful menstruation.

TREATMENT

Endocrine therapy

Hormone treatment may or may not be entirely scientific but according to various reports, even as a mere placebo the giving of a glandular preparation has good results. In one series of cases 90 per cent of the patients were entirely relieved by the administration of stilboestrol, this has the disadvantage that it suppresses ovulation and therefore the pituitary-ovarian balance may be disturbed.

Surgical measures

Randall and Odell state that the performance of hysterectomy, uterine suspension and presacral sympathectomy are unjustified procedures.

Bickers, W. (1941) *Amer J Obstet Gynec*, 42, 1023

Randall, J. H., and Odell, L. D. (1943) *J Amer med Ass*, 123, 735

DYSPEPSIA

CLINICAL PICTURE

In the Army

Hurst states that dyspepsia comprises up to the present time the largest single disease in the British Army. Hartfall considers that 60 per cent of the cases of dyspepsia in the Army are psychogenic, primarily or ultimately.

Hartfall, S. J. (1941) *Lancet*, 1, 124

Hurst, A. (1941) *Amer J digest Dis*, 8, 321

DYSPEPSIA, CARBOHYDRATE INTESTINAL

AETIOLOGY

Although intestinal flatulence is most often caused by carbohydrate dyspepsia, it

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may also occur without any deficiency in the digestive power of the stomach due to interference with the normal absorption of gas by the veins of the intestine. This is the cause of intestinal flatulence, of portal obstruction, and of chronic cardiac and pulmonary disorders. It may also be caused by local venous obstruction in chronic partial volvulus. It is quite unaffected by restriction of carbohydrates in the diet, and is generally made worse by aperients.

TREATMENT

The well known effect of the pressor substances of the posterior lobe of the pituitary gland in post-operative ileus suggests that it might be useful for these conditions. It is found that when care is taken to adjust the dose to the minimal requisite units ($\frac{1}{10}$ of a cubic centimetre) of pitocin, both the faeces and the gas are completely evacuated from the colon without discomfort. An injection can be given by the patient every morning if necessary and it does not lead to any ill-effects.

EAR DISEASES

FOREIGN BODIES AND INJURIES

Violence and explosions

Effects of blast

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When an explosion occurs in the air the effect on the tympanic membrane is two-fold in character. First there is a sudden initial and momentary increase of air pressure, secondly the air pressure gradually diminishes. The ear is thus subjected to the impact of a sinusoidal wave of an amplitude in keeping with the magnitude of the explosion. Ruedi has compared the sinusoidal wave to a wave of water with normal ridge and trough but with minor ripples on its surface, the latter are represented by the minor oscillations on the sound wave. The first or positive phase of blast is generally associated with rupture of the tympanic membrane but, as might be expected, the explosion must occur at a point fairly near to the affected ear. Sometimes the membrane may be completely detached from its basal ring, and the ear ossicles may be dislocated or broken. Partial deafness generally results. The structures of the inner ear may also be affected, so that the organ of Corti is disturbed and damage is done to the auditory nerve. It is not quite clear whether the damage to the inner ear arises in the positive or in the negative phase of the explosion, but it is obvious that the prognosis is much more serious when the inner ear structures are affected.

Ruedi, L. (1943) *Schweiz med Wschr*, 73, 913

ELECTROTHERAPY

DIRECT CURRENT

Ionization

In epidermophytosis

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Electrotherapy can be used as an almost specific treatment for the cure of the troublesome and prevalent condition of epidermophytosis. The areas infected are packed with cotton-wool pads soaked in 2 per cent zinc sulphate solution, the whole is covered with a pad soaked in 2 per cent zinc sulphate, and 4 to 5 milliamperes of direct current is passed through the pads, making the pad over the infected area positive, the time of application is 15 minutes. At the end of the treatment the area should be painted with friar's balsam. As a rule two treatments are sufficient for early cases.

LOW-VOLTAGE VARYING CURRENTS

Faradic currents

Constipation and obesity

The heavy, expensive and considerably cumbersome Bergonie apparatus for faradic stimulation of many groups of muscles simultaneously has been modified so that treatment practically identical with the complicated Bergonie treatment can now be given by any medical practitioner, masseuse, or even by the patient after suitable instruction. This chair is manufactured in London. Its advantages are compactness, incorporation of modern principles of making the current, and greatly improved electrodes, with consequent economy in prime cost, care and management. A great reduction in the expense of care and maintenance is also secured.

Thyratron valve

The spontaneous discharge of the Thyratron valve has now been made use of and adapted to impart a controlled voltage impulse to muscles under treatment. The results particularly after injury show a considerable improvement on the older forms of faradic stimulation.

HIGH-FREQUENCY CURRENTS

Short-wave current

Short-wave therapy was formerly regarded as the best for chronic infections of

the accessory nasal sinuses, there have, however, been some accidents with resulting permanent damage to the ears and to the pituitary by the passage of short waves through the sinuses, thereby overheating the structures at the base of the brain. To avoid this, the disk electrode supplied with most modern short-wave apparatus can be used, the indifferent electrode, a pad, being placed on the floor, or even in front of the patient, so that the short waves pass through the antrum or sinuses close to the disk electrode, and not through the whole thickness of the head. Intensive short-wave therapy given for middle-ear deafness, through from ear to ear, has resulted in a patient, formerly partly deaf, becoming completely deaf in both ears.

INDICATIONS FOR ELECTROTHERAPY

Infra-red rays can be used as a substitute for short-wave electrotherapy, particularly if a single thickness of lint or towel is placed on the patient. If a Kromayer lamp is available with a uvioi filter, since this is rich in one band of infra-red, it is also a useful substitute for short-wave therapy, but it must be used with considerable discretion. The Kromayer lamp can also be used for relieving the pain of osteoarthritis, to be effective it is necessary to use quartz rods with considerable pressure all around the area of the great trochanter. The method does not in any sense lead to a cure, but is a very potent means of alleviating the pain. To be effective, erythema doses must be given at least once a week for from 6 to 12 treatments, and the course must be repeated at least once a year.

Recent experience at an Emergency Medical Service Hospital has shown that direct current, using the positive as the active part, and the negative as the indifferent, can be utilized with benefit immediately after operations. The first treatment can be given before the patient has recovered from the anaesthetic. The positive electrode should be placed below (that is distal as regards lymphatic flow) the operation site and the negative electrode is placed above it at some distance, and a very small current of 2 milliamperes should be used for 15 minutes. The treatment should be repeated every day for 10 days, it will relieve pain, swelling and spasm.

Sulphanilamide, which is soluble to the extent of 0.8 per cent, can be used for the ionization of open wounds in order to enhance the activity of the drug. The positive electrode should be used, and a dose of from 4 to 5 milliamperes for 10 minutes is adequate.

The mercury vapour lamp can be employed for helping the healing process in first and second degree burns, it is also invaluable for the relief of pain in the early stages, and should be employed from the first days. The method and use are as follows. The area of healthy skin around the burn is isolated by means of black paper or some similar opaque substance. The burned area is then sprayed with sterile liquid paraffin, and is exposed to a full-sized mercury vapour lamp at 30 inches, for 2 minutes. The spraying with liquid paraffin should be renewed during the treatment if areas become free from this substance, as usually occurs, that is the treatment must be watched and the spray must be ready for use as soon as an area appears to be drying. The above dose is given every day, and the length of exposure is *not* increased for at least a week or 10 days, and may not require any increase at all.

It has been shown in the United States of America and elsewhere that a mercury vapour lamp, merely burning in places such as classrooms, wards, operating theatres, without actually shining on the patients, materially reduces the bacteriological content of the atmosphere, and in the case of classrooms it has been shown to minimize absenteeism and the incidence of winter colds and catarrh.

Ultra-violet light is also beneficial to night workers and underground workers. In one colliery the workers stand on a moving belt and are passed down through a gallery of ultra-violet lamps so that at the end of the belt, when they step off for their clean clothes, each man has had a standard dose on all sides of the body. The method has been found extremely helpful to output and for general improvement in health.

Ultra-violet light can also be used for assisting delayed union or non-union of bones, providing there is not a false joint. In such cases big doses are required, and a second degree of erythema is necessary if the correct reaction for bony union and regrowth is to be provided.

Guttmann has shown that a compound containing 28 per cent of chinizarin 2,6-disulphonic acid is effective when dusted on to the skin, for marking out the extent of injuries to cutaneous nerves. The subject is then placed in a radiant heat bath, and where sweating occurs the skin takes on a dark blue-violet colour. Various zones can then be mapped out, indicating (1) complete loss of sweating and sensation, (2) partial loss of sensation and diminished sweating and (3) the complete area of distribution of a nerve.

EMPHYEMA

ACUTE EMPYEMA

Clinical picture and diagnosis

Radiological examination

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The value of radiographs in the accurate diagnosis of acute empyema cannot be over-emphasized. An increasing number appear to become localized in unusual situations, such as the interlobar fissure or even at the apex, and in the former especially the physical signs are apt to be misleading. Radiographs in the antero-posterior and lateral positions make the condition clear. Another useful aid to diagnosis, especially giving assistance as to the best position for drainage, is to aspirate a reasonable quantity of pus, about 150 cubic centimetres, and to introduce about 100 cubic centimetres of air through the same needle. Radiograms taken in the upright, inverted and lateral positions will give the outline of the cavity by alteration in the fluid and air levels in the cavity. When basal, the cavity should usually be drained at a level of about one rib and interspace above the lowest level, to allow for post-operative rise of the diaphragm.

Treatment

General indications

Acute empyema due to different organisms requires different treatment in the early stages. Thus the pure pneumococcal empyema becoming localized early can be drained by rib resection soon after diagnosis is made, the streptococcal group in which localization occurs late should be treated by repeated aspiration until the purulent contents comprise at least seven-eighths pus after standing a specimen in a test-tube for 24 hours, and then should be treated by rib resection, lastly the fetid types which tend to cause widespread infection in the chest wall should be treated in the same way as the second group but the chest wall should be incised after the first aspiration, the wound packed and subsequent aspiration carried out through the incision after removal of the pack, which is replaced after completion of the procedure.

Operation

Drainage and expansion of lung—When rib resection has been performed at the right time, the question of airtight drainage is a matter of personal predilection but it is not essential for recovery. It has the advantage of infrequency of dressings and perhaps of greater rapidity in re-expansion of the lung but to a certain degree limits the movements of the patient. As soon as the cavity is reduced to a pleural track direct tube drainage into dressings can be adopted. It is important at this stage to determine the exact position of the tube in the remaining cavity in order to encourage free drainage and prevent the formation of pockets, which subsequently may become cut off from the main cavity and make further operation necessary. At regular intervals the cavity should be filled with fluid opaque to X-rays, and radiograms should be taken in the antero-posterior and lateral planes. By such means the gradual closure of the cavity is visualized, the relation of the drainage tube to the cavity determined and complete control of healing ensured. The most essential point is that the tube should not be removed until the pleural surfaces are in complete contact throughout the area of the previous cavity and the deep portion of the chest wall healed. Removal of the tube at too early a stage is responsible for more chronic empyema than any other single factor.

The value of modern respiratory exercises in the treatment of acute empyema has been only gradually realized. They are primarily directed to the abdominal muscles, which by alternate contraction and relaxation affect the corresponding diaphragmatic movements. Secondly the exercises are directed to controlled movements of the chest and more particularly to those portions of the chest wall overlying the empyema. Graduated movements in these two areas result in increased lymphatic drainage and blood supply and thereby assist in the absorption of the inflammatory products from the involved area and prevent the formation of fibrous tissue which does so much to restrict movement in neglected cases. Respiratory exercises should be begun within 2 or 3 days of drainage by rib resection and continued for 3 or 4 months, that is for some time after healing has occurred.

CHRONIC EMPYEMA

Treatment

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Some emphasis is still required in order to prevent the early employment of multiple rib-resection or so-called 'local thoracoplasty'. The first consideration is the assessment of the size of the residual cavity. A penetrating radiograph may enable this to be seen through the thickened pleura, but it is often of better value in such cases that the sinus should be dilated by the insertion of a sterile laminaria tent, this being left in for from 12 to 24 hours. If this opens the track into the cavity it can be easily filled with a radio-opaque solution and radiographed. If the cavity cannot be entered by this means, operation for the production of adequate drainage is performed. In either event drainage, irrigation of the cavity and negative pressure

by suction and respiratory exercises should be vigorously employed. In the great majority of cases, the cavity will become slowly obliterated and it is only after persistent failure of this method that any plastic procedure should be considered.

ENCEPHALITIS EPIDEMICA

AETIOLOGY

The virus

St. Louis encephalitis

St. Louis encephalitis and equine encephalo-myelitis—An annotation in the *Lancet* records that *St. Louis encephalitis* and *equine encephalo-myelitis* are now known to be closely related oecologically, although they are distinct immunologically. Both the eastern and western forms of *equine encephalo-myelitis* cause a highly fatal disease in human beings, especially in children. The viruses of the above diseases have the same vector, namely wild *Culex tarsalis* mosquitoes.

There is evidence that the mosquito *Culex pipiens* may have been implicated in the 1933 *St. Louis* epidemic. In 1938 two fresh-water breeders were present in places where *equine encephalo-myelitis* was prevalent, namely *Aedes vexans* and *A. triseriatus*, and in coastal areas *A. cantator* and *A. sollicitans* may have been vectors. There is no cross immunity between the *St. Louis* virus and those causing *encephalo-myelitis*, and *equine encephalo-myelitis* can occur concurrently with another neurotropic virus infection (Leading Article, *British Medical Journal*).

PATHOLOGY AND MORBID ANATOMY

The disease, *encephalitis Type A*, has been suspected to be due to a virus which has gained access to the central nervous system from the nasopharynx. The infective agent has not been demonstrated but is probably distinct from those causing epidemic *encephalitis Type B* of the Japanese (1912–29) and *St. Louis* (1933) epidemics, and Australian 'X' disease (1917–8). The age incidence in the former two is chiefly in adult life and in the latter in early childhood, but in none of these conditions are ocular palsies common, nor is the Parkinsonian state, and residual defects are rare.

TREATMENT

Benzedrine

According to Hoffman, by investigation of a single symptom of Parkinsonism, oculogyric crisis, which can be recorded by the patient, a more accurate impression of the effect of benzedrine on post-encephalitic Parkinsonism can be obtained, than by consideration of rigidity, tremor or sleep disturbance, each of which is obviously more difficult to assess. Seventeen patients were observed while under treatment with benzedrine in combination with stramonium, hyoscine, or similar drug, and a record was kept of their oculogyric attacks over a period varying from 2 to 12 weeks. Two patients were treated by benzedrine alone. The results were (1) good 4 (23.5 per cent), (2) moderate 5 (29.4 per cent), (3) poor 8 (47 per cent). Improvement was not recorded in the 2 cases treated with benzedrine alone but the patients improved with the addition of hyoscine and stramonium. These figures show some degree of improvement in 53 per cent of cases and indicate that benzedrine acts better if given with stramonium and hyoscine than if given alone. A careful watch must be kept on patients with cardiac disease or hypertension while they are under treatment with benzedrine.

Annotation (1941) *Lancet*, 1, 51

Hoffman, H. L. (1941) *Brit. med. J.*, 1, 816

Leading Article (1942) *Brit. med. J.*, 1, 441

ENCEPHALO-MYELITIS

SPONTANEOUS ENCEPHALO-MYELITIS

In addition to the virus infections, such as poliomyelitis, epidemic *encephalitis Type A*, rabies and herpes zoster, many others have recently been recognized—epidemic *encephalitis Type B* of Japan, *St. Louis encephalitis* of 1933 and Australian 'X' disease. Others, unlike poliomyelitis, the virus of which primarily affects man, appear to be infections of animals but capable of transmission to man, for example swineherds' disease—a benign lymphocytic meningitis, 'loup-ill' of sheep—possibly related to Australian 'X' disease, 'equine encephalitis' of North America (Webster and Wright), and the virus of acute choriomeningitis or benign lymphocytic meningitis found in mice.

Equine encephalitis

Equine encephalitis, epidemic in certain parts of North America, could be transmitted to man. Two serologically and epidemiologically different strains were recognized, the eastern and western types. During epidemics cases of *encephalitis* occurred among infants and children (Webster and Wright). Fothergill, Dingle, Farber and Connerley recovered the eastern strain of *equine encephalitis* virus from the brain of a child, aged 7, who died of *encephalitis*.

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Wesselhoeft, Smith and Branch report that, after an outbreak of equine encephalitis causing the death of 200 horses in south-east Massachusetts and Rhode Island, 24 cases in human beings were recorded. Of these 8 patients were admitted to hospital and all died.

Eklund and Blumstein report 6 cases of encephalitis in patients who had been in contact with sick horses. The symptoms were abrupt onset of headache, vomiting, dizziness, drowsiness and fever. Two patients died in from 4 to 5 days. Blood from 3 patients who recovered was tested against the western strain of equine encephalitis and the serum of one neutralized it.

Eklund, C M, and Blumstein, A (1938) *J Amer med Ass*, 111, 1734

Fothergill, L D, Dingle, J H, Farber, S, and Connerley, M L (1938) *New Engl J Med*, 219, 411

Webster, L T, and Wright, F H (1938) *Science*, 88, 305

Wesselhoeft, C, Smith, E C, and Branch, C F (1938) *J Amer med Ass*, 111, 1735

ENDOMETRIOSIS AND ADENOMYOMA

MORBID ANATOMY AND PATHOGENESIS

Histogenesis

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The hypothesis of lymphatic metastasis, originally suggested by Halban in 1924, has been supported strongly by Counsellor and by Gricouroff. It assumes that endometrium may be carried by the lymph channels to points outside the uterus. It covers all forms of endometriosis, and is consistent with the discovery of endometrium in lymph glands and vessels. If fragments leave the uterus and are arrested by an obstacle, they may grow if they do not meet any obstacle they are absorbed. The shorter the journey they have to make before arrest, the greater, probably, is their chance of survival. This is in keeping with the anatomical distribution of endometriosis, which is almost confined to a limited area in the middle of the body between the umbilicus and the perineum. The possibility of blood-vessel metastasis must be allowed, for lung endometriosis has been observed and is difficult to explain except in this way.

The chief objection to the hypothesis is that normal tissue does not metastasize. However, metastasis may occur with thyroid adenoma, and with chorionic and other tissue, and it is pointed out that proliferation of the uterine mucosa is a unique feature and may be compared with the conditions present in carcinoma.

CLINICAL ASPECTS

Treatment

According to Hirst there is a rational basis for prescribing androgens in endometriosis, but there is little in the literature with regard to the use of these and nothing about progesterone. The treatment of endometriosis is difficult as, either by surgical excision or radiological annulment of function, child-bearing is prevented. In an attempt to preserve reproductive function and at the same time to get rid of endometriosis Hirst has given intramuscular injections of testosterone propionate in large doses, and it is stressed that many months of treatment are essential if a substantial reduction of large endometrial masses is to be accomplished.

Counsellor, V S (1939) *Amer J Obstet Gynec*, 37, 788

Gricouroff, G (1939) *Ann Anat path med-chir*, 16, 751

Hirst, J C (1943) *Amer J Obstet Gynec*, 46, 97

ENDOSCOPY OF THE RECTUM

SIGMOIDOSCOPY

Instruments

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The Morgan-Officer type

An improved sigmoidoscope of the Morgan and Officer type is now available. It is made with tubes of 3 diameters, the two smaller ones are $\frac{3}{8}$ -inch and $\frac{1}{2}$ -inch respectively, so that they can be passed through a narrow anal canal or a stricture of the rectum. A magnifying attachment can be applied to the outer end of the instrument, and gives an excellent view, even with these very small sizes.

The colite type

Wakeley commends for sigmoidoscopy a tubular instrument made of colite (Vann Bros). The advantage of this type of sigmoidoscope is that the source of light is placed outside the tube so that the view of the area is unobstructed. Furthermore, diathermy instruments can be used safely, since the material is a non-conductor of heat and of electricity. Wakeley has had a stainless steel inspection mirror made for this instrument. This mirror is graded along the handle in inches upwards from the mirror. The walls of the sigmoidoscope being translucent, the mirror can be moved along the sigmoidoscope and early and accurate diagnosis assured. A complete examination can be done at one time.

Wakeley, C P G (1943) *Brit med J*, 1, 222

ENDOMETRIOSIS AND ADENOMYOMA—ENURESIS

ENDOSCOPY OF THE UPPER RESPIRATORY AND ALIMENTARY TRACTS

GASTROSCOPY

Use and indications

Within recent years there has been a considerable advance in the use of gastroscopy. So far as the Forces are concerned it has been possible to obtain much useful information, especially in dyspeptic conditions. Gill made extensive investigations with the gastroscope and in a report on 1,000 consecutive gastroscopic examinations in the Forces he observes that in gastric ulcer the gastroscope may reveal ulcers not otherwise demonstrable, the instrument is also an accurate and handy medium in the assessment of the degree of healing which is taking place. Gastroscopy can also be used in chronic gastritis, in which a very accurate picture can be viewed of the mucous membrane showing the type of gastritis, the degree of severity and so on. Treatment can be carried out thereafter on very accurate lines. The gastroscope is the only instrument which can disclose with any certainty the lesion of atrophy of the mucosa of the stomach. In addition to the above there is the big field of erosions of the stomach, radiology can rarely show these but the gastroscope allows them actually to be observed and it can be determined whether the condition is acute or chronic, once more also can appropriate and efficient treatment be decided upon.

Gill, A. M. (1943) *Lancet*, 1, 333

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ENEMAS AND COLONIC IRRIGATIONS

NUTRIENT ENEMAS

Absorption

As a result of recent investigations made by Mackenzie it has been shown that glucose, sodium chloride and predigested protein are absorbed from solutions introduced into the lower bowel, but there is great variation in the amount of glucose absorbed. So far as sodium chloride is concerned, the absorption is as great from the rectal surface as it is when it is given by the mouth. It was proved that there was absorbed a considerable quantity of predigested protein. This is an advance in knowledge greater than has been recorded for many years.

Mackenzie, J. W. A. (1943) *Arch. Dis. Childh.*, 18, 28

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ENTERIC FEVERS

THE ENTERIC GROUP OF FEVERS

Treatment

The three main essentials of treatment are fluids, vitamins and sodium chloride. Enteric fevers are all characterized by a degree of dehydration, which causes toxæmia, therefore from the beginning of the disease it is imperative that the patient should receive plenty of fluids. Water should be drunk between feeds and milk may be given as part of the hundred fluid ounces which should be the target for the day. In extreme cases normal saline solution with 10 per cent glucose should be given intravenously until 50 fluid ounces of urine are passed in 24 hours, the daily output being maintained at this level. Emphasis must be put on the effect of apple purée which, because of its pectin content, assists in the healing of ulcers. So far as the vitamins are concerned, as avitaminosis is blamed for the setting up of post-typhoid neuritis the feeds should contain ample amounts of vitamins. These also prevent haemorrhage, perforation of the bowel and the outbreak of skin lesions. With regard to sodium chloride, 10 grammes a day should be the intake, the nausea and vomiting of enteric fevers are controlled when there is enough sodium chloride supplied.

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TYPHOID FEVER

Treatment

Prophylaxis

Synthetic cream has been discovered as the origin of certain localized outbreaks of paratyphoid B. A common cause of infection has been a baker who is a carrier. The Widal test is not satisfactory, it is better to have repeated bacteriological examination of faeces and urine, the newer method of typing typhoid organisms which depends on their reaction to a specific bacteriophage is becoming firmly established.

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ENURESIS

CAUSATION

Gordon confirms that enuresis is commoner in allergic subjects, and suggests that the enuresis is due to abnormal psychological traits.

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TREATMENT

Urethral dilatation

Winsbury-White reports the results of treatment by urethral dilatation in 310 cases of enuresis in adults and children, the dilatation was performed under general anaesthesia, and the enuresis was improved in nearly all the patients.

Gordon, I (1942) *Brit med J*, 1, 357
Winsbury-White, H P (1941) *Lancet*, 2, 331

EPILEPSY

AETIOLOGY

Heredity and predisposition

Value of electroencephalography

425

Lennox, Gibbs and Gibbs state that statistics of the inheritance of epilepsy are open to errors due to ignorance of, or to the withholding of evidence by, the informants. For this reason a diagnosis of epilepsy based on objective laboratory evidence would be of the greatest help. Even more important would be the ability to demonstrate the 'predisposition' to epilepsy. Their experience with electroencephalography during 5 years convinced them that the electrical activity of the cortex represents a constitutional characteristic of the organism, and that the electroencephalogram offers a means of studying the hereditary factors of epilepsy. It must be remembered, they state, that the electrical activity of the brain is fluid and subject to constant change. Besides changing with age, the normal rhythm varies with the activity of the brain, with sleep or attention, or with pulmonary ventilation. On the other hand, the electroencephalogram of a person taken under standard conditions exhibits a certain constancy from day to day and a certain broad individuality. For example, a person with a record characterized by low voltage or by a fast or a slow rate tends to have the same type of record when examined repeatedly. The pattern of the normal record is not peculiar to any one person and may be indistinguishable from the record of many other persons. The most conclusive evidence in support of the hypothesis that the electroencephalogram is of genetic value is found in the records of uniovular twins, in each of 16 pairs of such twins the two members had similar tracings whether the tracings were normal or abnormal. Of 183 relatives of epileptics examined 60 per cent had definite dysrhythmia and 8 per cent had records which were classed as questionable. Therefore only 32 per cent of these near relatives had electroencephalographic records which were unmistakably normal. These findings should be compared with the results of examination of the group of 100 normal persons, none of whose relatives had a history of seizures. In this normal group 10 per cent had definitely abnormal records, 6 per cent questionably abnormal records and 84 per cent unquestionably normal records. The investigations showed that females were probably more predisposed than males to epilepsy.

PROGNOSIS

If an epileptic attack begins in a patient after the age of 40 years, and always allowing for a certain margin of error, it may be assumed that cerebral tumours, severe cerebral arteriosclerosis, G P I or other progressive disease is absent. A close study of 81 patients made by Nattrass showed that many in this category had recurrent attacks of epilepsy and no obvious signs of disease. Although the aetiology is not any clearer as the result of the investigations made, there are certain points in the prognosis which are useful. The first is that idiopathic epilepsy may be found in persons over the age of 40 years. Secondly, although fits may be the first symptom of intracranial tumour, the latter rarely occurs months or years before other symptoms and signs. Thirdly, the intellect and the health generally are little affected by the occurrence of epilepsy in later years of life.

DIAGNOSIS

Electroencephalogram

Method of recording

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The patient is seated with eyes closed in a darkened room and 6 electrodes are attached to the scalp over the two frontal, two motor and two occipital areas. These electrodes are connected with the grids of 6 Grass amplifiers which record on 6 brass ink writers. Records are taken for at least 20 minutes.

The value of electroencephalography in epilepsy is investigated by Williams, who considers that a non-specific diagnosis may be made from abnormalities in an electroencephalogram, but that a specific diagnosis depends upon clinical findings. About 40 per cent of epileptics have a normal electroencephalogram between fits. Walter considers that electroencephalography is of value in the diagnosis of latent epilepsy.

Electroencephalographic data

Reports made by authorities on the subject show that electroencephalographic investigation of epilepsy in all its types (*grand mal*, *petit mal*, mixed *grand mal* and *petit mal*, Jacksonian attacks and psychomotor attacks) prove that it is very difficult to correlate the findings with the clinical picture. Over 80 per cent of epileptics appear to have an abnormal electroencephalogram, and various conclusions may be drawn from the observations made. From 10 to 20 per cent of epileptics have a normal electroencephalogram and very often those with *grand mal* are in this category.

With regard to *petit mal*, the wave-and-spike pattern or the 3 per second wave is seen as a rule but an abnormal rhythm may be present only when there has been over-ventilation. Such rhythms may be found in other forms of epilepsy. There is no abnormal electroencephalogram which is pathognomonic of epilepsy. In every case therefore the whole history of the patient must be ranged with the electroencephalographic findings.

TREATMENT

Drugs

Epanutin

Sodium diphenylhydantoinate (epanutin) has been found to be of use in controlling seizures in some patients who do not respond to other forms of treatment and in those whose attacks occur often. This treatment is still in the experimental stage, but favourable reports have been published from America.

This drug is closely related to nirvanol. It produces toxic effects, for example ataxy, tremors, diplopia, dermatitis and purpura, but these disappear on cessation of treatment.

The optimal dosage varies. In patients above the age of 6 the initial dose should be 0.1 gramme 3 times daily, with or immediately after meals. The maximal dose is 0.6 gramme daily. Infants and children up to the age of 5 years should receive an initial dose of 0.1 to 0.2 gramme daily, this may be gradually increased to 0.3 or 0.4 gramme daily. Tullidge and Fox in a report on 43 patients said that 24 were completely freed from fits and 16 almost completely freed but the requisite dose was often so great that serious toxic reactions were set up and in about one-third of the cases the treatment had to be stopped. Epanutin does well in those with *grand mal* and psychomotor attacks. As a rule it is better to start with phenobarbitone and to turn to epanutin only when the former is unsuccessful.

Lennox, W. G., Gibbs, E. L., and Gibbs, F. A. (1940) *Arch. Neurol. Psychiat., Chicago*, **44**, 1155.

Natrass, F. J. (1943) *Brit. med. J.*, **2**, 481.

Tullidge, G. M., and Fox, J. T. (1942) *Lancet*, **2**, 6.

Walter, W. G. (1942) *J. ment. Sci.*, **88**, 110.

Williams, D. (1941) *J. Neurol. Psychiat.*, **4**, 257.

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EPISTAXIS

TREATMENT

In connexion with the treatment of difficult cases of epistaxis Davis describes in detail the blood supply of the nose and points out that the upper part is supplied by the internal carotid and the lower part by the external carotid. The volume of blood circulating in the nose was affected by changes in temperature and in the position of the head, in physical and mental exertion, and in emotion, patients with severe epistaxis should therefore be kept at rest in a sitting position, and change of temperature avoided. For spontaneous epistaxis in old people Davis recommended first sitting the patient upright with the head depressed and the nostrils compressed by finger and thumb. A pledget of wool soaked in 20 per cent cocaine hydrochloride should then be placed on the septum, and after its removal the nostril packed with the narrowest ribbon gauze soaked in 20 per cent cocaine hydrochloride solution with an equal quantity of adrenaline inhalant. After 10 minutes the gauze should be removed, then if the bleeding point is visible, it can be sealed by the dull red galvano-cautery or by gauze impregnated with ferropyrine powder. The gauze plug should not remain longer than 24 hours without removal or replacement. If local treatment fails, morphine sulphate $\frac{1}{4}$ grain should be given. For epistaxis associated with disorders of the blood, such as anaemia and leukaemia, Davis recommended the giving of blood transfusions, intravenous haemostatic serum and morphine. The inflated rubber bag was the best method of control in multiple telangiectasis.

Davis, E. D. D. (1939) *Brit. med. J.*, **1**, 721.

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ERYSIPELAS

TREATMENT

Sulphanilamide treatment in infants below the age of one month does not have any effect but infants above this age show results which indicate that cure is almost 100 per cent (Bruce and Chalkley). Otherwise, with this treatment in erysipelas in infancy the fall of temperature is much more sudden, steady improvement takes place early and erysipelas antitoxin and radiation by ultra-violet light are not required. The application of packs of magnesium sulphate is necessary only when there is a localized abscess. Very few complications are encountered and the average duration of the period spent in hospital is 50 per cent less than formerly was the case. Sulphanilamide should be given in doses of $1\frac{1}{2}$ grains per pound of body weight (0.2 gramme per kilogram) per day, divided into 6 or 8 equal doses, the first dose being twice the amount of those that follow. It is advisable to go on with this treat-

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- 441 ment for 3 or 4 days after the temperature reaches the normal level in order to prevent a recurrence
Bruce, J W, and Chalkley, T S (1943) *Amer J Dis Child*, **65**, 739

ERYTHEMA

CLINICAL PICTURE

Erythema due to internal causes

Erythema multiforme

- 442 Treatment—Keining and Oldach report favourable results of treatment with nicotinic acid amide in 24 cases of erythema multiforme, from 10 to 12 daily intramuscular injections of 100 milligrams were given, and impressive and rapid improvement occurred in the patients who were without rheumatoid or arthral symptoms
Keining, E, and Oldach, F A (1941) *Derm Wschr*, **112**, 285

ERYTHRAEMIA

Corrigendum

In Vol V, pp 180-1, in place of the paragraph on Irradiation and Indications, the following should be substituted

The idea of applying stimulating doses of X-rays to the spleen for the purpose of increasing the activity of the reticulo-endothelial system has now been abandoned in favour of depressant doses applied to the long bones, sternum and ribs. Daily treatment in small doses is preferable to weekly or monthly treatments with large doses. In polycythaemia vera it is now customary to irradiate the whole of the patient's body. In this wide-field or 'bath' treatment the dosage employed is a mere fraction of what is required when localized treatment is given to each area of involvement in turn. Moreover the patient is usually less upset by wide-field treatment and the benefit obtained appears to be more lasting. Skin reactions are not produced and the head may be safely included in the field of treatment without danger of producing epilation. It is advisable, however, to protect the gonads so as to avoid the risk of sterilization. When X-ray treatment is given the dosage must be carefully controlled by means of frequent blood counts and repeated clinical examinations. The immediate effects of treatment may not be obvious since several weeks may elapse before the erythrocyte count begins to fall. Once such a fall has begun it may continue over a period of weeks. It is important that treatment should terminate before there is any marked reduction in the erythrocyte count. If treatment is carried on for too long, there is a danger of producing aplastic anaemia. It is better to give too little than too much, because the course of treatment can always be repeated if too little has been given. It is probable that cases with a high platelet count are more particularly suitable for irradiation therapy than for phenylhydrazine treatment, since in such cases the tendency to thrombosis, already present, will be increased by treatment with the drug.

TREATMENT

Irradiation

- 443 Pierson and Smith describe the treatment of polycythaemia vera by roentgen irradiation of the entire body. The method is similar to that outlined by Sgalitzer, by Sanderson and by Hunter. The distance between the patient and the anode tube is from 2 to 2.5 metres, and there is no lead protection. From 30 to 40 roentgens are given at a treatment and the dose is repeated every day or every second day. Aluminium (1 millimetre) or aluminium (1 millimetre) and copper (0.5 millimetre) are used for filtration, with the latter the authors delivered 52 r in 20 minutes at a distance of 215 centimetres. The method appears to produce prolonged relief in most cases. Davidson confirms the efficacy of the method but considers that the above dosage may be excessive and may cause depression of the activity of the bone marrow.

Davidson, L S P (1942) Personal Communication

Hunter, F T (1936) *New Engl med J*, **214**, 1123

Pierson, J W, and Smith, C D (1940) *Amer J Roentgenol*, **43**, 577

Sanderson, S S (1936) *Amer J Roentgenol*, **35**, 670

Sgalitzer, M (1935) *Wien klin Wschr*, **48**, 675

FIBROSITIS

Corrigendum

In Vol V, p 286, 1st paragraph of section on Brachialgia, 2nd sentence should read: The structures most commonly affected are the subacromial bursa, the supraspinatus tendon, the sheath of the biceps tendon.

AETIOLOGY

Anxiety state

- 489 Gordon in an article on the known causes of fibrositis lays stress on the anxiety state which may act in 3 ways: (1) when pain is used as a symbol of

emotional discontent, (2) when the whole sensorium is over-sensitized as a result of acute emotional disturbance, (3) when chronic emotional disturbances produce endocrine and autonomic disturbances, through vegetative controlling centres on the hypothalamic region, these being followed by fibrositis

Bursitis

Olecranon bursitis is due to gout in a large proportion of cases

Pectoral fibrositis

Dixon emphasizes the importance of avoiding the erroneous diagnosis of angina of effort in cases of pectoral fibrositis. Symptoms of fibrositis may respond to nitroglycerin and so appear to confirm the mistake. If anginal symptoms are present in the absence of cardiovascular symptoms, fibrositis should be looked for, cardiac abnormalities, however, may be associated. The fibrositis should be treated by breaking up the nodules with the fingers at least 4 times a week for 2 weeks.

Palindromic rheumatism

Hench and Rosenberg discuss a new recurrent disease, namely 'palindromic rheumatism' (arthritis, peri-arthritis, para-arthritis) which does not apparently cause any residual changes, it has been studied at the Mayo Clinic since 1928. The authors discuss the evidence for and against the allergic aetiology of palindromic rheumatism and report 34 cases. The characteristic clinical features are multiple afebrile attacks of acute arthritis which usually involves one joint, with pain, swelling, redness and disability, the symptoms generally appear suddenly and last only for a few hours or days. There is a transient inflammatory polymorphonuclear exudate in the joint cavity and surrounding tissues, with little or no constitutional reaction. In the authors' series, 70 per cent of the patients were between 20 and 39 years of age and the disease lasted for several years, with an incidence of from 2 to 250 attacks per year. Para-arthritis and skin nodules (usually on the hands) appeared in a few cases (9 per cent).

Cohen in 1911 and in 1913 recorded a somewhat similar condition which he termed 'angioneural arthrosis', and in 1939 Kahlmeter described cases of allergic rheumatism.

Cohen, S. S. (1911) *Trans. Coll. Phys., Philadelphia*, **33**, 309.

— (1913) *Trans. Ass. Amer. Phys.*, **28**, 739.

Dixon, R. H. (1938) *Brit. med. J.*, **2**, 891.

Gordon, R. G. (1940) *Ann. rheum. Dis.*, **2**, 89.

Hench, P. S., and Rosenberg, E. F. (1941) *Proc. Mayo Clin.*, **16**, 808.

Kahlmeter, G. (1939) *Acta med. scand.*, **102**, 432.

FILARIASIS

FILARIINAE

Corrigendum

In Vol. V, foot of p. 313, the paragraph on distribution should be replaced by the following: 'The distribution of this filaria, as at present known, is Java, Sumatra and other islands of the Malay Archipelago, southern India, Ceylon and southern China.'

Wuchereria bancrofti

Pathology and morbid anatomy

Napier, Das Gupta and Rao have performed sternal puncture, both by day and by night, in 53 cases of filariasis, but in all there were more microfilariae in the peripheral blood than in the sternal puncture fluid. There is not therefore any evidence that microfilariae shelter in the bone marrow during the day or that they are destroyed there.

491

Filaria malayi

The life history of the mosquitoes (*Mansonioides*) concerned in transmission of this organism is an excellent example of scientific oecology, because the larva is provided with a special respiratory siphon in order to enable it to absorb oxygen from the roots of *Pistia stratiotes*, a water plant on which it lives. The prevention of the disease is therefore intimately connected with the eradication of the plant.

The parental forms of *Filaria malayi* have now been found and described by Rao and Mapleston, and will henceforth be known as *Wuchereria malayi*. This nematode is practically identical with *W. bancrofti* in nearly every characteristic. The females are quite indistinguishable. The males, as in *W. bancrofti*, have 9 pedunculated caudal papillae, but the spicules of the new species are more slender and delicate and lack the transverse corrugations on the stout portion, seen in *W. bancrofti*. In addition it is pointed out that the embryo has a quite distinctive morphology and that it develops also in a distinctive intermediary host, *Mansonioides annulifera*.

CUMULATIVE SUPPLEMENT 1945
ONCHOCERCINAE

Onchocerca volvulus

- 492 Onchocerciasis has become a medical problem in Tanganyika Territory and in Kenya. McMahon made a preliminary investigation of part of the South Kavirondo district in Kenya at an altitude between 4,000 and 5,000 feet. Skin snips of 605 men, women and children were examined and 51 per cent were positive for *O. volvulus*. The fly, *Simulium naevei*, was found to carry the infection, and on dissection of 557 flies developmental forms of onchocerca were found.

McMahon, J. P. (1940) *Trans. R. Soc. trop. Med. Hyg.*, **34**, 65.

Napier, L. E., Das Gupta, C. R., and Rao, S. S. (1940) *Indian J. med. Res.*, **28**, 605.

Rao, S. S., and Maplestone, P. A. (1940) *Indian med. Gaz.*, **75**, 159.

FLUKE INFECTIONS, INTESTINAL

FLUKES

- 496 Three new species of trematodes have been reported from the intestinal tract of man. Sandground reports the third instance of *Plagiorchis javensis* infection in a Javanese in Batavia. Only one individual trematode was found, measuring 2 millimetres in length by less than 1 millimetre in breadth, this has been provisionally named *P. philippinensis*. The first record was that of Africa and Garcia who found 5 specimens of a plagiorchis in the small intestine of a native of the Province Ilocos Sur, Philippines.

Sandground, together with Bonne, has renamed the echinostome of Celebes, *E. lindoensis*. This species resembles *E. revolutum* but is characterized by the possession of 37 collar spines. Larval development was found in natural infections of a small planorbid, *Anisus (Gyraulus) sarasinorum*, and the metacercariae in several pulmonate snails *Viviparus javanicus rudipellis* and also in the mussel *Corbicula lindoensis*, both of which form a regular part of the native diet. The parasites are rapidly expelled by tetrachlorethylene medication and as many as 250 worms have been recovered after a single treatment. This same parasite has been reported also from Mexico by Rodriguez in a description of 5 infections in man, one of which was experimental. In each case the diagnosis was parasitic colitis, eggs being found in the stools together with *Ascaris*, *Enterobius* and, once, with *Taenia saginata* and *T. solium*.

The intermediary hosts in Mexico are *Limnaea attenuata*, *Physa oscularis* and *Planorbis tenuis*. Experimental infections have been reproduced in ducks and pigeons by feeding them on these snails. Hsu found 2 small trematodes in the small intestine of a Chinese in Peiping who had died of myelogenous leukaemia. This species is described as *Euparyphium jassyense*, but it has been pointed out by Szidat that, as originally described by Leon and Ciurea, it is identical with *E. melis*. According to Beaver development of this species probably takes place in tadpoles, and it is suggested that these larvae were eaten by the patient described above by Hsu.

FASCIOLOPSIASIS

Life cycle

- 497 According to Kuang Wu the cercariae of *Fasciolopsis busku* may become encysted on almost any plant that grows in stagnant water and as many as 20 encysted metacercariae may be found on a single leaf, on *Salvinia natans* and *Spirodela (Lemna) polyrrhiza*, plants which float on the surface.

A new intermediate host for *F. busku*, *Segmentina trochoideus*, is recorded by Buckley.

Geographical distribution

F. busku is reported by Buckley to be a common human infection in parts of Assam, 59.7 per cent of 221 stools showed the infection.

Treatment

McCoy and Chu treated 129 children whose faeces showed eggs of *F. busku* with hexylresorcinol. The dosage was 0.4 gramme for children under 7 years of age, to 1 gramme for those over 13. Re-examination of the patients from 2 to 3 weeks later showed that eggs were absent in 54 per cent, and that in all but 5 per cent their numbers had been reduced by at least one half.

FASCIOLIASIS

- 498 Manson-Bahr and Walton in a review of the incidence of *Fasciola hepatica* in man in Great Britain state that it is commoner than is generally supposed. They report a case in which *F. hepatica* was found in the common bile-duct of a woman who had never been out of Great Britain. A surprising fact was the absence of eggs from the faeces and the absence of a definitive eosinophilia.

HETEROPHYES HETEROPHYES

Pathology

- 500 Infestation with these flukes causes a few minor symptoms. Intermittent diarrhoea has been described.

FLUKE INFECTIONS, INTESTINAL—FOOD

- Beaver, P. C. (1941) *J Parasit*, **27**, 35
 Buckley, J. J. C. (1939) *J Helminthol*, **17**, 1
 Hsu, H. F. (1940) *Chin med J*, **58**, 552
 Kuang Wu (1937) *Ann Parasit hum comp*, **15**, 458
 McCoy, O. R., and Chu, T. C. (1937) *Chin med J*, **51**, 937
 Manson-Bahr, P., and Walton, J. (1941) *Brit J Surg*, **28**, 380
 Rodriguez, I. L. (1940) *Echinostoma revolution* studied for the first time in Mexico as a Parasite of Man Thesis Mexico
 Sandground, J. H. (1940) *Rev Med Trop Parasit*, **6**, 207
 — and Bonne, C. (1940) *Amer J trop Med*, **20**, 511

FOETUS DISEASES, MALFORMATIONS AND MONSTROSITIES

ABNORMAL CONDITIONS OCCURRING IN LIVING FOETUS

Skin*Ehlers-Danlos syndrome*

Sullivan reports a case, in a man aged 24 years, of the Ehlers-Danlos syndrome (cutis laxa, cutis hyperelastica, dermatorrhexis and indiarubber man), with transient paralysis of the left vocal cord. The patients are often contortionists. The abnormality is very uncommon, the primary characteristics are (1) hyperelasticity of the skin, (2) hypermotility of the joints, (3) a tendency to abnormal and deficient scar formation, (4) small tumours of the skin, there may also be associated acrocyanosis and chilblains. The cause is unknown but the condition is considered to be a congenital dystrophy. The author's patient, who had undergone operation for disease of the urinary bladder, became hoarse, with a temperature of 104° F, and had almost total paralysis of the left vocal cord, this cleared up in 5 days. X-ray examination of the neck and aortic arch did not show any evidence of disease. The patient's physical condition showed characteristic signs of the Ehlers-Danlos syndrome with double-jointedness and a very loose skin, although tumours were not present, the voice was stated to be high and harsh, and there was a history of similar short episodes of difficulty in speaking. The cause of the transient paralyses of the vocal cord is unknown, their association with the Ehlers-Danlos syndrome may have been a coincidence. The syndrome has not been described previously in conjunction with a neurological disorder.

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DOUBLE MONSTERS

Classification*Nomenclature of double autosites*

Heterosexual conjoined twins—Another case of thoracopagus twins in which one foetus (right) had the external genitalia of a female and the other (left) those of a male, with normal penis 2 centimetres long, and urethra, as well as rudimentary scrotum—in which, however, no testes could be felt—was delivered by Szendi of Debrecen, Hungary, in February, 1938, this case will be published in full, but he kindly stated that the gonads of each foetus were ovaries, and that each also had a uterus and tubes, there was no prostate in the apparent male. In addition, the adrenal cortex of each foetus contained the fuchsinophil cells found in pseudo-hermaphrodites (see Vol V, p 367). The right foetus, therefore, was a normal female, and the left was a feminine pseudo-hermaphrodite. But, since pseudo-hermaphroditism is a Mendelian character (see Vol V, p 367), the difficulty of explaining the monozygotic origin of this thoracopagus still remains.

510

Situs inversus in one member only of a pair of conjoined twins

There seems to be no doubt that situs inversus in the right member alone of a pair of conjoined twins is not uncommon, especially in thoracopagi. This phenomenon is somewhat difficult to explain. Ordinarily situs inversus occurs as a Mendelian recessive and therefore its occurrence in one member only of such a pair should be conclusive evidence of their binovular origin. On the other hand, the facts that when such situs inversus was present in conjoined twins it always occurred in the right member only, and that it was sometimes found in one member only of a pair of ordinary separate identical twins (Dubreuil-Chambardel, and others), led to the conclusion that in such cases it was a stereoisomerism, that is, a mirror-image phenomenon. But, if this were the case, such stereoisomerism would be expected in all conjoined twins, as well as in all identical twins, this is not the case.

Dubreuil-Chambardel, L. (1927) *Pr med*, **35**, 1157

Sullivan, J. D. (1942) *Arch Neurol Psychiat, Chicago*, **47**, 316

FOOD

MAJOR CONSTITUENTS OF FOOD

Nitrogenous constituents

It has been demonstrated that there are 10 amino-acids which cannot be manufactured by the rat from other amino-acids and which must be supplied as such. But it has not been demonstrated that these acids are essential for man.

513

- 515 Zinc**
Zinc is now known to be one of the physiological elements and essential for life. It is part of the enzyme carbonic anhydrase which assists the liberation of carbon dioxide in the lungs and probably has a part to play in the formation of hydrochloric acid in the stomach.

VITAMINS

- 516 Vitamin C**
Among the vitamins, the supply of vitamin C requires to be considered most. Despite war conditions there has been very little scurvy in Great Britain during the years 1939-44. Before citrus fruits made a welcome reappearance the main supply of vitamin C was from vegetables and potatoes and from home-grown fruits in problematical amounts. It has to be emphasized that the potato as it is available all the year round is the most reliable source of vitamin C. In an age in which people are led to believe that by swallowing a tablet they can keep themselves well supplied with vitamins it is advisable to remind patients that they should take their ordinary food, and they should be told to eat more potatoes and green vegetables. These vegetables should be cooked quickly and served at once, they contain not only vitamin C but vitamin A and calcium.

THE AVAILABILITY OF CERTAIN FOOD CONSTITUENTS

- 517 Calcium**
The work of the last few years has confirmed and extended the knowledge which was at our disposal in 1937 about the availability of calcium. It has been shown that the rachitic agent in cereals, which was discovered by Mellanby in the early 1920's, is phytic acid. If sodium phytate is added to a puppy's diet, the animal can be made to develop rickets, and experiments on human beings have shown that there is enough of this substance in brown bread to prevent the absorption of much of the calcium in the rest of the diet.

The whole question of available iron has again been thrown into the melting-pot. It has been shown, in the first place, that the organic iron in meat is rendered available when it is heated during the process of cooking, and it has even been shown that some of the iron in unheated haemoglobin can be absorbed. Liberation of this iron for absorption is probably the work of bacteria in some part of the intestine. In the second place, it has been suggested that phytic acid may interfere with the absorption of iron as it does with that of calcium, so that the inorganic iron in food—particularly in whole cereals—is not necessarily all available. For the present, at any rate, it looks as though those who are interested in iron metabolism would have to go back to the old convention of measuring and working in terms of the total iron in the foodstuffs rather than fractionating this into available and unavailable iron.

FOOD REQUIREMENTS AND INTAKE

- 518 Minimum and optimum requirements**
Calcium, phosphorus, iron and iodine are the main inorganic elements which have to be watched so far as an ideal dietary is concerned. Calcium and phosphorus are required by adults at the rate of about a half-gramme a day. Children require more—0.8 gramme for those from over 6 months to 2 years of age. An adolescent may have up to 2 grammes and a pregnant woman requires from 1.5 grammes to 3 grammes a day. Vegetables do not give up calcium easily and the best sources of calcium are milk and cheese. So far as iron is concerned, it must be soluble and ultrafiltrable. Only about 6.5 milligrams is required daily. With regard to iron, it is reported that endemic goitre in Michigan has been reduced almost to nil by the use of iodized salt.

FOOT, DISEASES AND DEFORMITIES

PAINFUL CONDITIONS

- Metatarsalgia**
Pathology
526 The underlying pathology of the condition described variously as weak foot, painful foot, foot fatigue, strained foot and so on is still undetermined, and the mechanism of the less obvious lesions is not clear. Hallux valgus, hammer-toe, corns and similar conditions are well recognized, but the difficulty arises in the case of the foot which does not display any gross deformity or disproportion and which shows evidence of functional breakdown when an additional strain is put on, as for example when a man or woman is directed to go into the Forces or into a factory. There are two main opinions held, those which are based on physiological or muscular grounds and those which have a purely anatomical or ligamentous foundation. Thus one group of observers thinks that the muscles lose control of the foot so that an unusual strain is thrown upon ligaments, bones and other structures, and then the machine fails. The second group regards the human foot, as it is used only for locomotion,

FOOT, DISEASES—FROST-BITE AND TRENCH FOOT

as a part of the body which has become altered by evolutionary demands, therefore when there is a failure, the passive structures in the foot are primarily concerned, the muscular effect being secondary

Clinical picture

The main site of pain is the sole of the foot, but it has to be remembered that it is the calf muscles which control the posture of the foot. The foot may be tender and show swelling. In order to explain the fatigue which is to be found in the ligaments and fasciae of the foot it has been suggested that there may be a reflex beginning in the sensory nerve endings of these tissues, inflammation would be a natural reaction.

Pressure ischaemia may ultimately have its effects on the feet, in on those who have to bear the maximum weight on certain points, particularly under the heads of the metatarsal bones. This is almost certain to be the cause of the pain and tenderness felt in the sole of the foot at the end of a long shift in the factory. Another factor is passive congestion, apart from the effects of varicose veins, swelling and congestion of the foot may be an important factor, for various reasons the vascular return may be poor so that pain and swelling of the foot are the rule at the end of the day.

Treatment

With pathology doubtful, treatment must be empirical. Common sense should prompt the practitioner to apply reasonable measures in the treatment. The foot must be broken in to any new type of activity, whether this be marching or standing for a long time at a bench, the foot may have to be trained also for inactivity as well as for activity. Correct stance is another important aspect of the treatment, a good stance is one in which the trunk is braced well back so that the centre of gravity of the body falls through the stout bones of the posterior half of the foot back to the heel, the forepart of the foot being used merely to conserve the balance. The feet should be directed straight forward and they will then also fall naturally into a position of slight inversion.

FROST-BITE AND TRENCH FOOT

AETIOLOGY

Greene^{2,3} discusses the causes, prevention and treatment of frost-bite and the associated conditions of trench foot, shelter foot and immersion foot which are caused by various factors including cold and damp. Excessive warmth during recovery, circulatory stagnation, wind, anoxia, dietetic deficiencies and trauma are also important contributory causes. Treatment should be directed towards avoidance of trauma and infection. The part should be rested, the feet if involved being raised and the patient being treated as a stretcher case. Amputation is seldom required and is never urgent.

528

Frost-bite may follow even momentary exposure at low temperatures, especially at great altitudes or in a high wind. Some authors consider hypovitaminosis to be a causal factor.

The essential morbid change is damage to the vessels and muscles followed by transudation or even by rupture. Individuals vary in the surface temperature at which their skin begins to freeze, ranging from -2.2°C to -25°C . This is due to variation in the factor of supercooling, a capacity to go below freezing-point without solidifying. This capacity to supercool is increased by leaving the skin unwashed for a week or by rubbing in olive oil, and is abolished by immersion in water. An important factor in frost-bite at high altitudes is lack of oxygen. The tachycardia of high altitudes is associated with a decrease in the minute volume of the heart. Administration of oxygen increases the amount of circulating blood and has a marked warming effect. Greene¹ recommends inhalation of pure oxygen from a face-piece on the earliest signs of frost-bite at high altitudes.

CLINICAL PICTURE

Immersion foot

Webster, Woolhouse and Johnston record their experiences in treating 142 cases of immersion foot from the North Atlantic, the duration of exposure having varied from 30 hours to 22 days. Treatment was based on the hypothesis that 'the original trauma results in an intense vasodilatation, together with actual damage to the vessel walls and damage to peripheral nerves or end organs. A vicious circle is thus established with resulting oedema and transudation of serum and blood, all of which further contribute to the already present oxygen debt in the involved part. This latter in turn leads to an increase in oedema and transudation of whole blood.' The aim of treatment was to reduce by refrigeration the metabolic demands of the part until local vascular conditions had returned to normal. This was accomplished (1) by the application of a towel to the feet, surrounded in turn by ice-bags (changed every 4 hours), oiled silk, thick cotton padding, and rubber pillow-cases, or (2) by

exposing the feet to the blast of a fan, through the blades of which cold water was sprayed on the feet, or (3) by exposing the feet to cool room temperature. Whatever the method, further essentials were the strictest asepsis and elevation of the feet.

Results

Pain disappeared within an hour, and oedema rapidly subsided, an interesting finding being the return of oedema to feet from which the ice-bags had been removed, although they were still elevated. The contents of blebs or extravasations were reabsorbed. In all minimal, mild and moderate cases the patients recovered completely after desquamation of the skin of the feet (average stay in hospital 30 days). It was noted that when these patients began to walk they showed a flat-footed springless gait. This may have been due to paralysis of the small muscles of the sole of the foot, which were not investigated. Of the severe cases 7 patients were discharged after the loss of minimal amounts of superficial tissue, in the remaining 8 tissue loss was more extensive. The authors emphasize the deplorable results of rapid warming, and agree that sympathectomy is contra-indicated because the vessels are already fully dilated. Vitamin deficiency and dehydration were not observed in these subjects. It is suggested that in severe cases heparin might prevent or minimize thrombosis in the vessels near the affected area.

High altitude frost-bite

Aerial warfare has brought yet another type of frost-bite to add to the list. If an airman takes off his gloves for a moment when he is at a certain altitude he becomes affected with a type of frost-bite in which the fingers become waxy white, insensitive, stiff and hard and are maintained in the extended position. Even if the patient has been in a warm room for several hours afterwards the original condition may be maintained and in fact the loss of sensation may continue for several weeks. In severe cases there is a wet type and a dry type of frost-bite. The wet type is characterized by many blisters which coalesce to form one large blister, situated on the dorsum of the hand, and commonly on the fingers, this skin dries after about 3 days and is shown as a slough, subungual haemorrhages causing loss of the nails. In the event of epithelial regeneration the skin may take nearly a year to become normal again. The dry type shows a very tense skin which is like ground glass and underneath the tissues take on different colours varying from grey to black, mummification is a common sequel, especially of the terminal phalanges, the demarcation is defined soon and very clearly—probably within a month (Davis, Scarff, Rogers and Dickinson).

TREATMENT

Specific

When frost-bite has occurred, the application of any source of heat above normal body temperature is dangerous, for the stagnant circulation is incapable of dissipating this heat. One satisfactory way of warming the patient is by close contact with another human body. Increasing the transudation by warmth and rubbing must be avoided, for the same reason alcohol should not be given, owing to the peripheral dilatation caused by it. Rubbing the damaged tissues is liable to increase the harm. Complete rest of the frost-bitten part is essential. It should be cleaned and wrapped in dry sterilized dressings and many layers of wool, being handled throughout with extreme gentleness. Tetanus antiserum should be given as the devitalized tissue is particularly subject to infection. Amputation should be delayed as long as possible, because, if gangrene develops, the line of demarcation may appear to be much more proximal than the true level. This point is also emphasized by Rabut.

Lewis describes the normal and injurious effects of cold upon the skin and underlying tissues with observations on the phenomena and reactions involved and he recommends that the lesions should be treated like similar lesions resulting from heat, namely local redness, wheal, flare, blister, cellular exudate and necrosis, after strictly controlled thawing.

Andrews warns against treatment by friction and recommends that blisters be left intact and painted with 1 in 1,000 acriflavine solution, with suitable protective dressings.

- Andrews, M. C. (1941) *Brit med J*, 1, 763
- Davis, L., Scarff, J. E., Rogers, N., and Dickinson, M. (1943) *Surg Gynec Obstet*, 77, 561
- Greene, R. (1940)¹ *Lancet*, 1, 303
- (1941)² *ibid*, 2, 689
- (1942)³ *Practitioner*, 148, 38
- Lewis, T. (1941) *Brit med J*, 2, 795, 837, 869
- Rabut, R. (1939) *Pr méd*, 47, 1683
- Webster, D. R., Woolhouse, F. M., and Johnston, J. L. (1942) *J Bone Jt Surg*, 24, 785

FUNGIOUS DISEASES—GASSING AND POISON GASES IN WAR

FUNGIOUS DISEASES

Vol. V
KEY NUMBERS

RINGWORM INFECTIONS

Ringworm of the flexures

Treatment

Shapiro, working with a very large amount of material in a military hospital in the Transvaal, found that Non-staining Iodine Ointment B P C was unmistakably superior to Whitfield's ointment in controlled comparisons (one foot as compared with the other and so on) and sometimes, but not always, superior to Castellani's paint

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Barber emphasizes the importance of preliminary exfoliation and for this purpose he uses the following lotion: salicylic acid 1 drachm and spirit to 1 ounce. The lotion is applied morning and evening, and compound powder of salicylic acid (B P C) is then used. At the end of 2 weeks exfoliation is well established and the lotion may be omitted. Then he uses Whitfield's ointment at night and in the morning the following lotion: equal parts of weak solution of iodine (B P) and industrial methylated spirit (B P), the above powder being used afterwards.

MONILIAL INFECTIONS

Clinical picture

Liston and Cruikshank found that 49 out of 200 consecutive cases of leucorrhoea were due to *Monilia albicans*. This is important in view of risks to a baby. They note that aphthous vaginitis in adults receives scant notice in text-books.

536

Treatment

Treatment with a 1 per cent aqueous solution of gentian violet is satisfactory. Signs in the mouth usually disappear after the first application. It has been liberally applied to the mouth in a suspected case of thrush-oesophagitis in the hope that it would reach the affected areas, the results were encouraging.

DERMATOPHYTIDES

Aetiology and clinical picture

Microsporum lanosum may produce inflammatory or non-inflammatory lesions of the scalp. When it produces non-inflammatory lesions they may be clinically indistinguishable from those due to *M. audouinii*. Since the *M. lanosum* and *M. audouinii* ringworms respond differently to treatment, a mycological study of the dermatophyte is often of the utmost importance. These strains have been described in detail by Dowding and Orr and by Conant.

544

M. lanosum may attack the scalp, body or beard, also the hair and glabrous skin of animals. It commonly produces inflammatory lesions, curable by local applications of fungicides. Dowding and Orr have repeatedly isolated *M. lanosum* in Alberta from non-inflammatory scalp lesions, which can only be distinguished from those due to *M. audouinii* by mycological methods.

Cleveland cured 26 non-inflammatory cases of tinea capitis (which clinically he took to be due to *M. audouinii*) by local treatment alone. Subsequently he sent infected hairs from 6 of these patients with dry scaly lesions, and 1 with suppurating lesions, to Dowding and Orr. Seven cultures from them proved to be *M. lanosum*, thus explaining Cleveland's apparently surprising results.

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GASSING AND POISON GASES IN WAR

VESICANT GASES

Mustard-gas

Effect on eyes

If a droplet of mustard-gas falls into the eye, immediate irrigation with water diminishes the resultant injury. Irrigation neither affords any benefit if it is delayed for more than 5 minutes, nor is it of the slightest use if inflammation of the eye has already begun to develop after exposure to air containing mustard-gas vapour, since there is always a long delay before symptoms make their appearance. It is therefore useless to adopt irrigation as a routine measure when a suspected case of mustard-gas poisoning is first seen, such treatment wastes time which would be better devoted to various essential measures such as removal of contaminated clothing, cleansing of the skin and other procedures, and should be used only when there is reason to think that a droplet of mustard-gas may have actually fallen into the eye within the previous 5 minutes. When conjunctivitis has

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developed, a few drops of a non-irritating antiseptic should be instilled 4 times daily, a 2.5 per cent solution of albucid soluble, one of the sulphonamide derivatives, has been suggested for this purpose. The stronger antiseptics should be avoided. If discharge is copious it should be washed away before instilling the antiseptic. Stress is laid on the value of atropine if blepharospasm and pain are pronounced. The use of liquid paraffin is contra-indicated during the first few hours on account of its tendency to dissolve and to spread the toxic agent throughout the conjunctival sac later than this its use is of value in the prevention of the lids from becoming adherent. All but the mildest cases should, if possible, be seen by an ophthalmologist in order to obtain early diagnosis of material injury of the cornea.

The most comprehensive paper on the subject is that of Mann and Pullinger. Experimental lesions from doses of varying intensity at different anatomical sites were induced in large numbers of rabbits' eyes. The effects, minor and major, with the course of events in the corneas, were critically recorded over many months. These results were classified and correlated to those from clinical cases of two types among human subjects: (1) early, from accidental gassing of varying severity, and (2) late, from war casualties of 1917-8. A very complete picture of the effects of mustard-gas on the eyes has thus been built up, and allowing for the accepted fact that lesions are developed 10 times more quickly in the rabbit's eye than in man's, the work has shown that the pathological changes induced by lesions at the corneo-scleral junction run similar courses in the one case in from 12 to 18 months, in the other from over 10 to 15 years. The development of the destructive ulceration with its striking clinical characteristics has been watched and explained in its various stages by the experimental work with rabbits. Although agents other than mustard-gas will produce lesions similar to many of those recorded, the characteristic corneal blood islands and varicosities and the late ulceration in the cholesterol deposits have not been induced by anything but mustard-gas. Similarly, there are not any known ocular lesions in man which produce the changes typical of the late results of severe mustard-gas injury.

The work has shown that the reaction of the eye in rabbit and in man is dependent on the dose, whether from droplet or vapour, and on the anatomical situation of the lesion. The severe late sequelae are seen as results of the initial damage to the eye, and not as effects from any continued action of mustard-gas or its breakdown products in the cornea. Since it is very difficult to assess the dosage involved in the mustard-gas injury to any one human eye, the value of treatment is hard to judge, so that at the present stage of our knowledge the question of treatment is unsatisfactory. Prevention of ocular injury from mustard-gas is thus of paramount importance. The protection given by the Army eye shield is considerable, and that of the accurately fitting and properly used respirator much greater, if not complete.

Skin

Triple dye has the same disadvantage as tannic acid in the treatment of blistered areas because excessive exudation of fluid during the first day or two tends to float off the scab. For burns of moderate size treatment with amyl salicylate, as originally suggested for the treatment of thermal burns, helps to dry up the exudation, reduces the surrounding oedema and erythema, and relieves pain and irritation. After the area has been cleansed with a non-irritating antiseptic, such as dettol, 20 per cent solution, and the blisters punctured, a pad of gauze or lint, soaked in amyl salicylate and well wrung out, should be applied, covered with Cellophane and cotton-wool and lightly bandaged. The dressing should be changed once or twice daily, and when the wound is dry some other dressing, for example crude neutral cod-liver oil, should be substituted. Notwithstanding its disadvantages, treatment with one of the tanning agents may perhaps prove desirable in extensive burns in view of the possibility of shock caused by toxic absorption. Amyl salicylate should not be used for burns of the face because its vapour irritates the eyes. If the burns become septic mildly antiseptic baths may be useful, as well as application of powdered sulphanilamide to the wound.

Systemic effect

Mustard-gas, if absorbed in sufficient quantity by the lungs or skin, is capable of causing serious degenerative changes in the bone marrow and pronounced leucopenia. Such a leucopenia may accentuate the danger attributable to secondary infection of the damaged lungs or skin.

Genital organs

Amyl salicylate should not be used for the treatment of burns of the genital organs since it is irritant in this situation, although excellent for use elsewhere on the body or limbs. Irritation can be relieved by the use of lotions such as 1 per cent acriflavine, or calamine lotion containing 1 per cent of carbolic acid. Ointment should be avoided as it renders it difficult to keep the parts clean and is bound to prove troublesome if actual vesication develops. A warm bath is also a very good method for relieving irritation of the genital organs.

GASSING AND POISON GASES IN WAR

Lewisite

The treatment of lewisite injuries should be in general the same as for mustard-gas. If a sufficient amount of liquid lewisite is absorbed from the bare skin, symptoms of acute arsenical poisoning may result, and experiments on animals have shown the following pathological changes in such cases: haemorrhagic inflammation of the gall-bladder and bile-ducts, necrosis of the liver, inflammation and degeneration of the kidney, albuminuria, anaemia, increase in blood urea, and concentration of the blood as in shock. From such experiments it would appear that 1.0 cubic centimetre of liquid lewisite would prove a fatal dose for man from skin absorption, and that 0.3 cubic centimetre would cause serious illness. Such heavy contamination of the bare skin should, however, occur only in exceptional circumstances.

Aqueous bleach cream, or ointments containing chloramine-T, hydrolyse and oxidize lewisite into compounds which are no longer vesicant although they may still be toxic on absorption. Treatment with hydrogen peroxide (20 volumes) or hyperol (urea peroxide) solution (20 grammes to 100 cubic centimetres of water) carries the oxidation still further to products of lower toxicity, and thus lessens the serious symptoms which might otherwise result from absorption, so long as the treatment is applied within $\frac{1}{2}$ –1 hour of contamination. The affected area should be thoroughly swabbed with the peroxide, and a dressing kept wet with the same solution should be applied for an hour, or longer if possible. A systemic toxic effect in the shape of leucopenia and atrophic changes in the bone marrow has been stated to occur after the application of large amounts of liquid mustard-gas to the skin. Liquid mustard-gas, however, is less rapidly absorbed than liquid lewisite by the skin, and, since the decontamination treatment by bleach cream or antigas ointment containing chloramine-T can destroy the toxic properties of mustard-gas, the prompt application of such treatment should largely eliminate the possibility of subsequent systemic effects due to the absorption of the poison as such.

LUNG-IRRITANT (ASPHYXIANT) GASES

Treatment*Phosgene*

Transfusion of serum or plasma (normal or concentrated) fails to restore the blood volume in animals when haemoconcentration occurs during the development of pulmonary oedema, but accentuates the pulmonary oedema and thus may accelerate death. Transfusion is therefore inadmissible as a method for combating the shock-like condition of grey cyanosis which is liable to result in man when pulmonary oedema is caused by the acute lung-irritant gases.

Attempts to reduce the permeability of the lung tissue to fluid and thus to diminish the pulmonary oedema by raising the calcium content of the blood, whether by parathyroid extract or by the injection subcutaneously or intramuscularly of calcium gluconate, have proved fruitless. Large doses of calcium chloride or gluconate are damaging to the tissues and may cause sloughing of the skin.

OTHER POTENTIAL WAR GASES

Hydrocyanic acid (HCN)

Hydrocyanic acid was used in shells to some extent in the 1914–18 war but did not prove an effective offensive agent owing to the fact that, although the action of the gas is very rapid when it is present in sufficiently high concentration in the air, low concentrations can be borne for a considerable time without serious results. The gas owes its poisonous properties to the fact that it interferes with the oxidation processes of the cells in all the tissues and for this reason acts as a direct poison of the nervous system. Cases of accidental hydrocyanic acid poisoning sometimes result from the use of this substance as a fumigant for destroying vermin.

Symptoms follow one another in rapid sequence: giddiness, confusion, headache, indistinct sight, palpitation, pain in the chest and over the heart, laboured respiration, unconsciousness, convulsions, and failure of the respiration and finally of the heart. In large doses it causes immediate unconsciousness, dilatation of the pupils, a few gasping respirations and death with or without convulsions.

Treatment

Treatment consists in immediate removal to fresh air. If the respiration has stopped or is very weak and gasping, artificial respiration must be instantly applied. If the patient can be resuscitated recovery will be complete.

Hydrocyanic acid poisoning was dealt with more fully in Vol. XII, pp. 85–8 and 151.

Sulphuretted hydrogen (H₂S)

An attempt was made to use this gas in the 1914–18 war as an offensive agent, but only on a small scale. Accidental cases of poisoning with this gas have occurred in sewers (See also Vol. XII, pp. 150, 151).

With high concentrations this gas may act as rapidly as hydrocyanic acid as a

Leucocyte count

Hynes reports the results of a number of serial leucocyte counts in German measles, and shows that leucocyte counts are sufficient to distinguish between this disease and scarlet fever or glandular fever, but not between it and measles

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GLAUCOMA

PRIMARY GLAUCOMA

Clinical picture

The onset of glaucoma is in most cases insidious and must be searched for carefully in any person over 40 years of age complaining of neuralgic headaches. Sometimes the symptoms are very slight and appear negligible to the patient. Failure to recognize them and to establish early treatment leads to disastrous consequences. The most important sign is the raised intra-ocular pressure which is detected only by careful observations made on a patient suspected of glaucoma, the observations should be made in the morning and evening, or at such times as symptoms are experienced. Generally the disease is bilateral and it is imperative to keep the patient under observation for the remainder of his life.

The results of surgical treatment are, on the whole, satisfactory in 70 per cent of cases, although the prognosis depends much upon the stage at which the disease is effectively treated and other factors peculiar to the individual case. Much patience, tact and fortitude are needed by the medical practitioner in piloting the patient through all the changing phases of his mental reactions to the disease, beginning with his amused indifference to the situation and ending, in some instances, with his pathetic terror as realities begin to cast their dark shadows over him.

Treatment

Use of prostigmine bromide in America

The action of prostigmine bromide (neostigmine bromide) in glaucoma is spoken of in favourable terms by Montalvan. He points out that operation is not always successful and that modern opinion tends to the view that medical treatment should first be tried. The drug, which is the dimethylcarbamic ester of metahydroxyphenyltrimethylammonium bromide, has been used in a series of 28 cases, including chronic primary glaucoma, glaucoma secondary to quiescent anterior uveitis and absolute glaucoma, the total number of eyes treated was 52. Twenty-three had not received any previous treatment (group 1), in 6 the tension had been controlled by miotics other than prostigmine (group 2), in 20 other eyes miotics had failed (group 3), so far as the 3 remaining eyes were concerned the previous history was not given. All patients were treated initially by instillation with a 5 per cent solution of prostigmine bromide. In cases in which tension was successfully controlled, the strength of the solution was halved after a few days. The upper limit of normal tension was taken as 30 millimetres Hg on the Schiotz tonometer. It was found that prostigmine bromide controlled the tension in 78 per cent of the first group, 33 per cent of the second and 25 per cent of the third group. Subjectively prostigmine bromide appeared to cause less interference than did other miotics with normal use of the eyes.

Furmethide

Experiments designed to compare the effect of furmethide (furfuryltrimethylammonium iodide) with that of mecholyl (acetyl-3-methylcholine chloride) plus prostigmine bromide in lowering the ocular tension have been carried out in America by Uhler in cases of glaucoma. Furmethide is a choline derivative which is not attacked by cholinesterase. (1) Twenty-three patients with primary acute glaucoma and an intra-ocular pressure which measured over 40 millimetres Hg by the Schiotz tonometer were treated by instillation of a 10 per cent solution of furmethide, whereas 43 received mecholyl and prostigmine. It was found that although furmethide was slightly more effective in lowering intra-ocular tension than were mecholyl and prostigmine in late cases, it was less effective in early cases, that is

those cases in which the field defect was less than 30 degrees in any meridian and the blind-spot not enlarged more than 10 degrees in any diameter (2) Eighteen cases of acute secondary glaucoma were treated with furmethide and 19 with mecholyl plus prostigmine, neither drug had any effect on tension (3) Twenty patients with primary chronic glaucoma in whom tension was not controlled by pilocarpine were treated with furmethide In 10 the tension fell to normal but the low level was not maintained No general or local ill effects were observed during long periods of administration

Montalvan, P (1943) *Amer J Ophthal*, 26, 57

Uhler, Ella M (1943) *Amer J Ophthal*, 26, 710

GLYCOSURIA

Corrigenda

In lines 10 and 11 of the paragraph on Fehling's test on page 594 of Vol V substitute 'potassium' for 'sodium', to read as follows solution B contains 176 g of Rochelle salt and 77 g of potassium hydroxide in water to 500 c cm

For paragraph 3 on page 597 substitute the following Laevulosuria after a dose of laevulose may occur either (1) because the blood sugar rises too high, or (2) because the threshold of the kidney is set at a lower level than usual

For paragraph 5 on page 597 substitute the following

(ii) The normal threshold of the kidney for laevulose is set considerably lower than for dextrose, and 'sugar' often appears in the urine when a laevulose tolerance test is performed (Spence and Brett) Laevulosuria sometimes occurs spontaneously in healthy people, especially if they have been eating plenty of fruit When the nature of the reducing substance is known it is unnecessary to institute any treatment

On p 598, line 11, delete 'glycine as', to read 'combined with glycuronic acid'

On p 598, last paragraph, 4th sentence, substitute the following Each drop is followed by a deep purple, or green, or blue colour which disappears at once

Substitute the following end reference for Harrison, G A (1930)

Harrison, G A (1937) *Chemical Methods in Clinical Medicine their Application and Interpretation with the Technique of the Simple Tests*, p 117, 2nd ed London

GOITRE AND OTHER DISEASES OF THE THYROID GLAND

PATHOLOGY OF THE THYROID GLAND

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The recent developments in knowledge of goitre and diseases of the thyroid gland deal mainly with the relation of the thyrotrophic hormone of the anterior lobe of the pituitary gland to the function of the thyroid gland and to exophthalmos

Thyrotrophic extracts of the anterior pituitary on injection into animals and man cause a rise in basal metabolism and hyperplasia of the thyroid But, even if the injections are continued, the metabolism returns to normal and the gland undergoes involution Associated with this regression in the activity of the thyroid, it is possible to demonstrate the presence in the serum of the injected animal or man of an action inhibitory to the thyrotrophic extract of the anterior pituitary It has not been possible to demonstrate the presence of this anti-thyrotrophic action in the serum of cases of toxic goitre and, although it is accepted that the activity of the thyroid gland is normally under the control of the anterior pituitary, there is no evidence so far that there is excessive anterior pituitary activity in cases of toxic goitre, although the occasional association of toxic goitre with acromegaly is suggestive that such may occur In a proportion of the animals receiving injections of thyrotrophic extract of the anterior pituitary, exophthalmos is produced This occurs even in animals from which the thyroid has been removed Further, in those in which thyroid hyperplasia and a rise in metabolism have been produced, the exophthalmos occurs in the stage of regression when the metabolism has returned to normal and the gland has undergone involution The production of exophthalmos is therefore independent of the function of the thyroid and may possibly be enhanced by a diminution in, or absence of, thyroid activity In cases of toxic goitre, exophthalmos may sometimes arise or increase in severity after subtotal thyroidectomy, and it is commonly observed that the degree of exophthalmos is not directly related to the severity of toxicity These clinical observations are in agreement with the experimental production of exophthalmos in animals receiving thyrotrophic extract of the anterior pituitary So far, exophthalmos has not been reported as being produced in human beings by injections of such extracts, and although there seems considerable evidence that exophthalmos is the result of anterior pituitary activity rather than of activity of the thyroid, the parts played by disturbances of these glands in the exophthalmos of toxic goitre are not yet clear

There is evidence that the exophthalmos which results from injection of thyrotrophic extracts of the anterior pituitary in animals is prevented by division of the

cervical sympathetic fibres, and lessened by the administration of thyroxine and of iodine. Sympathectomy has been successfully employed in the treatment of severe exophthalmos in man which continues after subtotal thyroidectomy

SIMPLE GOITRE

Treatment

Iodized salt

The Sub-committee of the Medical Research Council recommend that a national policy of adding iodized salt to all common salt in domestic and culinary use be adopted. One part of potassium iodide should be added to 100,000 parts of common salt

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Memorandum of the Goitre Sub-committee of the Medical Research Council (1944) *Lancet*, 1, 107

GONORRHOEA

Vol VI

AETIOLOGY

That there are more cases of chronic gonorrhoea today is the result of two factors. The first is ineffective use of sulphonamide drugs, the second is inadequate dosage and improper application. Sometimes there is drug intolerance, and all things considered, there is a greater chance of the acute stage merging into the chronic

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BACTERIOLOGY

Improvement in cultural methods

The tendency of sulphonamide treatment to suppress symptoms in an important proportion of uncured cases has caused increased attention to be concentrated on methods of diagnosis and tests of cure which depend fundamentally on discovery of the gonococcus. The result has been a general improvement in the cultural methods employed in laboratories and consequent confirmation of the view held by those workers who for many years have employed good media that by culture a very important proportion of gonococcal carriers are detected who would be missed if reliance were placed only on microscopical examination of stained smears.

Weiss and Colvin in a review of the literature relating to the examination of 13,783 specimens for the presence of gonococci, show that these organisms were present in 4,482 of the specimens, both smear and culture were positive in 2,817, smear only was positive in 471, and culture only was positive in over a quarter of the positive cases.

Sulphonamide resistance

Sulphonamide resistance has been a major factor in failure of sulphonamide treatment of gonorrhoea, when a sulphonamide is used the doses given at the beginning of the treatment should be large, because, in the first place, the infecting organism may be relatively resistant or, in the second place, in a relatively inaccessible focus, and if for either or both these reasons the remedy reaches the organism in a sublethal concentration it may make it still more resistant.

Intractable infections are by no means always due to a sulphonamide-resistant strain. The infection which proves resistant in one partner of an infected couple may react readily to the same drug in the other partner (Harkness).

GONORRHOEA IN MALES

Clinical picture

In a few of the chronic cases the infection remains limited to the anterior urethra in which residual foci of infection may persist in some of the minute urethral glands. An inflammatory or soft stricture is thus readily produced and can be recognized on urethroscopy. The condition responds well to instrumental dilatation which is undoubtedly necessary and which cannot be replaced by any variety of chemotherapy. In most of the chronic cases the infection spreads to the posterior urethra, involving the prostatic ducts and the alveoli of the gland, in some cases the seminal vesicles also become involved.

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Treatment

General treatment

If one sulphonamide drug fails to effect a cure in gonorrhoea, trial should be made of another member of the group, but 10 days at least should be allowed to elapse between the courses of treatment, the dose should be 5 grammes a day for 6 days, evenly spaced. It is essential that plenty of fluid should be taken. The patients should also call to see the doctor every other day so that any unusual signs or symptoms may be noted early. In the case of inexplicable exacerbation the possibility of a reinfection must not be forgotten.

MacKenna working under military conditions with patients in hospital, has reported good results in a scheme in which 22 grammes of sulphapyridine were given in 48 hours, at the rate of 5, 4, 3, 2 and 8×1 gramme at 4-hourly intervals, day and night. In these intensive schemes strong emphasis is laid on the importance of the

patients taking very large quantities of liquid to prevent precipitation of the drug in the kidneys with resultant haematuria, anuria and possibly death

Fairbrother, Aymer and Ashton have reported on the absorption of sulphapyridine in 18 patients treated on the lines just described and in 21 treated with a rather smaller dosage in the same time, namely 3, 3, 2 and 8×1 gramme at 4-hourly intervals. The concentration of the drug in the blood was approximately the same in both series, ranging from about 4 milligrams per 100 cubic centimetres to over 14 milligrams, in most cases a concentration of from 8 to 10 milligrams per cent was reached and was maintained for from 36 to 44 hours. They did not find any close correlation between the blood level and the clinical progress, they thought also that a lower dosage would result in much the same concentration and that a lower concentration would serve for the destruction of the gonococci.

Laird has made a systematic investigation of 6 different schemes of dosage with sulphapyridine and obtained the best results with one in which 1 gramme was given every 4 hours, day and night, for 4 days, the patient also had urethral irrigation with potassium permanganate solution, 1 in 8,000, and was made to drink not less than 7 pints of fluid a day. With this course the cures out-of-hand were 91 per cent in 209 cases, the next highest cure rate being 84.5 per cent. Laird considers that omission of irrigation and restriction of fluids are detrimental to success with the above form of treatment.

One great advantage of the sulphonamide treatment of gonorrhoea is the reduction of complications both local and metastatic which its use has brought about, and here it is possible to foresee through its agency far less sterility of both males and females than was the case before the introduction of this form of treatment.

The above selection of experiences will have given the impression of a rather wide difference of opinion on methods of conducting the chemotherapy of gonorrhoea and it seems desirable to attempt to evolve from them some guiding principles. First it appears evident that there may always be a risk of the gonococcus acquiring some resistance to the remedy unless it is destroyed quickly by its agency. This indicates that the best plan of treatment is one which gives the attack every advantage possible from the outset, and that therefore the highest dosage which the patient can tolerate should be prescribed at once. Conversely it means that a timid dosage from the start may result only in the development by the germ of complete resistance to chemotherapy. Two other factors also favour a scheme of high dosage and the shortest period of treatment compatible with eradication of the disease. One is the greater probability of the development of blood dyscrasias from long drawn out treatment than from short and sharp courses with relatively heavy dosage, the other is that under a prolonged timid dosage scheme of treatment patients are more apt to discontinue treatment whilst still infectious than under a short and sharp scheme.

Fever therapy

T A B vaccine—Short-period high pyrexia produced by the injection of foreign protein such as T A B vaccine or a febrile session of longer duration set up by physical means, has had good results. T A B vaccine was given as an intravenous injection of 25,000,000 organisms followed from 2 to 3 hours later by an additional injection of 25,000,000 organisms. This caused a temperature to be produced which ascended to a peak of 103° F or more which lasted for 3 hours.

Mechanical methods—In resistant gonorrhoea the Kettering Hypertherm has been used widely with success. Patients were submitted to a pyrexia which lasted for from 6 to 8 hours, in these cases a sulphonamide drug should be given during the 24 hours which precede the hyperthermia.

Inductothermy—Pyrexia of a duration similar to that mentioned above can be obtained by submitting the patient to treatment by short-wave and high-frequency current in an Inductotherm cabinet. Sulphapyridine should have been given previously for a day, partly by the intravenous route.

Penicillin

The early results from the use of penicillin are very encouraging, penicillin has been proved in America to have success in cases of chronic sulphonamide-resistant gonorrhoea.

Local treatment

In addition to chemotherapy it is still sound practice in chronic cases to give daily urethro-vesical irrigations with potassium permanganate, 1 in 8,000.

Infected areas of the genito-urinary canal must be freely drained, otherwise sulphonamide treatment may be hampered. If prostatic drainage is unsatisfactory gentle massage should be carried out and daily irrigation treatment with potassium permanganate, 1 in 8,000, given. Physiotherapeutic methods may also be employed. When the prostate gland is tender and nodular and when there is little secretion without any pus cells it is a sign that there is a closed focus.

Tests of cure*Tests in sulphonamide treatment*

Most workers stress the importance of stringent tests of cure, as sulphonamide treatment, when it fails, is apt to result in a rather long period of clinical latency which may give the impression that the patient is cured, but Mahoney, Van Slyke and Wolcott have not found this to be so after treatment by sulphathiazole, and do not think that bacteriological tests of cure are necessary when this remedy has been used

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Clinical picture GONORRHOEA IN ADULT FEMALES*Blind para-urethral ducts*

Gjessing has examined the urethras of 35 female corpses and as a result has found, besides the well-known Skene's tubules and Morgagni's lacunae, that in some bodies there are single median ducts in the posterior wall, as described by Schuller in 1883, and in others double ones. He also saw some with blind ducts in the anterior wall of the urethra. All these are important possible harbours for the gonococcus

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Superior right abdominal complex in gonococcal adnexitis

Mauro gives the following account of such cases of gonococcal perihepatitis. In a woman with salpingitis, under the influence of gynaecological manoeuvres or apparently spontaneously, a syndrome develops, localized in the right hypochondrium, or sometimes in the left, there is pain radiating also to the epigastric region, the subscapular, and the right shoulder with abdominal muscular rigidity and cutaneous hyperaesthesia. In the right pleural *cul-de-sac* signs of inflammation are found, sometimes with a serous effusion. Some general symptoms such as gastric pains and vomiting also occur. There is not much fever. Jaundice is rare. He discusses the possible routes of spread, and considers that dissemination by the blood vessels is unlikely, the possibility of lymphatic spread is interesting but does not explain all cases, he considers direct spread along the parietal peritoneum to be the most likely

Diagnosis

Clinical examination should be made in the lithotomy position with adequate illumination, and urination should not have occurred for at least one and preferably two hours previously, so that urethral massage will show whether urethritis or skenitis is present or not

Cultural tests

Recently the American Neisserian Medical Society stated that lubricant should not be used on instruments or fingers employed for taking specimens for cultural tests of gonococcal infections. Lubricant is one of the reasons for lack of success with the cultural method in some venereal disease clinics and laboratories

Cohn, Steer and Adler¹ state that the easiest method of obtaining specimens from the vagina is to insert an ordinary female glass catheter containing a small amount of normal saline into the vagina and move it about there. Smears and cultures may then be made from the mixture picked up by the catheter. Cultures are more likely to grow the organism if the material is smeared straight away on to the culture medium and placed in an incubator within the subsequent 4 hours. Smears taken soon after the monthly period, when there has not been any recent douching, are the most likely to give a positive result. The blood should be taken for a complement fixation test for gonorrhoea (G F T). A positive G F T may be taken to indicate either that the woman has had a straightforward attack of gonorrhoea, and has put up a resistance to the infection, or that some complication such as pelvic organ involvement is present. Gonorrhoeal arthritis may produce a positive test, especially if the infection is longstanding, but many patients with gonorrhoeal arthritis give a negative G F T in the blood. The diagnosis however in the latter type of case is made by the presence of the organism most commonly in the urethral smears

Treatment

Sulphonamide treatment is not as successful in the female as it is in the male. The main reasons may be summarized as follows: (1) omission to seek early advice, (2) the possibility of urethral as well as vaginal infection, (3) menstrual complications, (4) hidden gonorrhoea—without symptoms

A bimanual pelvic examination should be made on the woman at each attendance and whenever any clinical sign of even slight swelling of the tubes or tenderness in the fornices is detected, adequate drainage of the uterine cavity through the vagina should be ensured. This is easily performed under gas and oxygen, or hexobarbitone, anaesthesia in the out-patient department, although rest in bed for a few days is preferable. The cervix is dilated up to 10 Hegar size and a number 10 or 12 Jaques's rubber catheter is inserted and 20 cubic centimetres of sterile glycerin injected well

CUMULATIVE SUPPLEMENT 1945

up into the uterine cavity. If convenient the catheter is stitched to the cervix with a silkworm gut suture and instillations of sterile glycerin are given daily for 4 days, after which the catheter usually slips out easily. This treatment, either alone or combined if considered necessary with sulphonamide therapy, may be used with success in any case except when there is extensive pelvic peritonitis or a pyosalpinx present. In this event the opinion of a gynaecological surgeon should be sought.

Sulphonamide treatment

Sulphadiazine is the drug of choice in early conditions, the dose is $7\frac{1}{2}$ grains given 4 times a day for 12 days. Sulphathiazole is a suitable alternative, given in a dosage of 1 gramme for every pound of body weight daily for 2 days and then in lessened doses for from 3 to 5 days subsequently. Another method is to give 20 grammes in a 5-day course.

Tests of cure

Clinical and pathological examinations as previously described must be entirely negative when made on 3 occasions directly after consecutive menstrual periods, and subsequent to the cessation of all treatment. This is a high standard but a most necessary one.

VULVOVAGINITIS IN CHILDREN

Aetiology

- 578 Cohn, Steer and Adler², as a result of a long research on vulvovaginitis, have concluded that lavatory seats are not a source of danger. They have never seen a case of cross-infection, although lavatory seats were used indiscriminately by children with acute discharges and by healthy children. Moreover, during the whole course of their investigation no epidemic of vulvovaginitis occurred in Greater New York although it was known that girls with vulvovaginitis attended schools for months before being brought under treatment. The authors think that important causes of cross-infection are sex play and sex curiosity which begin in children much earlier than is commonly imagined. Lewis, who was associated with this investigation, thinks that the lavatory seat as a source of infection is a mere bogey and agrees with Nelson that children should be excluded from school only so long as there is free discharge.

Treatment

The two great therapeutic resources in gonococcal vulvovaginitis continue to be the oestrogenic hormones and the sulphonamides.

Oestrogenic hormones

Results of oestrogenic therapy must be evaluated in the light of the experience of Cohn, Steer and Adler², who left 42 girls suffering from gonococcal vulvovaginitis without any treatment whatever and found at the end of 28 weeks that 78.8 per cent of them were completely free from signs of the disease. Lewis, formerly a strong advocate of oestrogenic treatment, now thinks its effect is only symptomatic.

Sulphonamide drugs

Hynes has worked out the doses of sulphanilamide required to produce the effective concentration of from 4 to 10 milligrams per 100 cubic centimetres in the blood. They are

0 - 3 mths,	0.125 g	every 4 hrs	= 0.75 g	in 24 hrs
3 - 6 "	0.25 g	" 6 "	= 1.0 "	" "
6 - 18 "	0.25 g	" 4 "	= 1.5 "	" "
1½ - 4 yrs,	0.5 g	" 6 "	= 2.0 "	" "
4 - 8 "	0.5 g	" 4 "	= 3.0 "	" "
8 - 12 "	1.0 g	" 6 "	= 4.0 "	" "
Adults	1.0 g	" 4 "	= 6.0 "	" "

Cohn, A., Steer, A., and Adler, Eleanor L. (1940)¹ *Vener Dis Inform*, 21, 208.

— — — (1941)² *Amer J Syph*, 25, 329.

Fairbrother, R. W., Aymer, C. A., and Ashton, C. W. (1942) *Lancet*, 1, 464.

Gjessing, H. C. (1939) *Acta derm-venereol*, Stockh, 20, 59.

Harkness, A. H. (1943) *Lancet*, 2, 116.

Hynes, M. (1940) *Lancet*, 1, 261.

Laird, S. M. (1942) *Lancet*, 1, 463.

MacKenna, R. M. B. (1941) *Brit med J*, 1, 958.

Mahoney, J. F., Van Slyke, C. J., and Wolcott, R. R. (1941) *Vener Dis Inform*, 22, 425.

Mauro, E. (1938) *Pr méd*, 46, 1919.

Weiss, T. E., and Colvin, S. H., Jun. (1941) *South med J*, 34, 1102.

GOUT**Corrigendum**

Vol VI, on page 39, 5th paragraph The statement that uric acid is generally present in the blood in organic combination with thymic acid is now open to question

579

PATHOLOGY

The view that impairment of the power of the kidney to excrete uric acid is the chief causal factor in gout has been modified as a result of the work of Folin and his collaborators. In this it appears that gouty patients are able to excrete uric acid injected into them as rapidly and as completely as normal controls. Moreover, gouty persons can in the early stages concentrate uric acid in their urine to as high a level as can normal individuals. Bauer and Klemperer give support to this theory, in chronic leukaemia, polycythaemia and other conditions associated with an increased destruction of nucleo-protein in the body, hyperuricaemia is accompanied by increased excretion, but the opposite is the case in gout.

It has been demonstrated that the blood urate concentration influences the urine urate concentration in normal individuals and that urate clearance is increased with free diuresis, a matter of considerable importance in the gouty subject. The influence of cinchophen in increasing urate clearance is well recognized but it is not so generally known that this effect is abolished by denervation of the kidney, indicating that the autonomic nervous system has a regulatory function in uric acid excretion. The reduced inability to excrete uric acid in normal amount is present in gouty subjects before there is any demonstrable disease of the kidneys, and in the earliest stages there may be normal uric acid levels in the blood and normal power of excretion between attacks, but it should be noted that this is denied by some authorities. Gradually definite renal disease is manifested and the lesion is a vascular sclerosis of a type met with in other parts. Hypertension is however a late development and the blood pressure in early cases is often lower than the average for the age.

TREATMENT**General and spa treatment**

According to Buckley, colchicum remains the most effective remedy. It does not appear to affect the excretion of urates, and might be combined with sodium salicylate, which has such an effect. Inclusion of sufficient alkali to keep the urine alkaline and thus prevent deposition of uric acid in the urinary tract is advisable as in the following prescription:

Colchicum wine	-	-	-	-	15 minims
Sodium salicylate	-	-	-	-	20 grains
Potassium bicarbonate	-	-	-	-	30 grains
Liquid extract of liquorice	-	-	-	-	10 minims
Peppermint water to	-	-	-	-	1 ounce

This dose might be repeated in an hour and continued at intervals of 2 or 3 hours until symptoms become less acute, the interval might then be increased 3 times a day, and this dosage continued until the attack has subsided or symptoms of over-dosage, such as nausea or diarrhoea, occur.

An adequate supply of fluids—water, weak tea and fruit squashes—to ensure free diuresis is also of considerable importance in order to assist in urate clearance, and due note of this factor must be observed in the dietetic regime. Since certain mineral waters have a pronounced diuretic action this may be taken advantage of and is certainly a factor in producing the beneficial effects of spa treatment.

Bauer and Klemperer (1942) *Diseases of Metabolism* London

Buckley, C. W. (1938) *Med. Pr.*, 197, 482

Folin, O., Berglund, H., and Derick, C. (1924) *J. biol. Chem.*, 60, 361

GRANULOMA, ULCERATIVE**AETIOLOGY****Donovan's organisms**

Dienst and his colleagues and Greenblatt and his colleagues do not believe that the Donovan bodies, which in their view are the cause of granuloma inguinale, have ever been cultivated on artificial media. They suggest that it is probably a sporozoon which is highly selective for its host and that it reproduces only in mononuclear endothelial cells. They have never succeeded in inoculating any experimental animal with this organism.

580

TREATMENT

Ross treated a case seen in Liverpool, but in which the disease had been contracted a month previously in Brazil, with sulphapyridine, no other general treatment was employed, 6 tablets, each of 0.5 gramme, were given daily for 14 days, and immediate improvement followed. In 5 days the ulceration was half healed, in 10 days epithelialization was in an advanced state, and in 14 days was complete, during the subsequent 11 days there was not any recurrence.

CUMULATIVE SUPPLEMENT 1945

Grace reports that treatment by sulphonamides yields most satisfactory results. Sulphathiazole has been found to produce slightly more rapid effects than sulphanilamide, possibly because the dose of the former is nearly double that of the latter.

Dienst, R. B., Greenblatt, R. B., and Sanderson, E. S. (1938) *J infect Dis*, **62**, 112

Grace, A. W. (1941) *Bull N Y Acad Med*, **17**, 627

Greenblatt, R. B., Dienst, R. B., Pund, E. R., and Torpin, R. (1939) *J Amer med Ass*, **113**, 1109

Ross, A. O. F. (1939) *Lancet*, **1**, 26

GUINEA-WORM DISEASE

EXPERIMENTAL INFECTIONS

Experimental infection of dogs

581

Moorthy and Sweet have published a further report on their experimental infection of dogs with guinea-worm, described in Vol VI, p. 65. This paper includes reports on the necropsies of a further 3 of the dogs infected orally and of 2 controls. From one dog 11 adult female guinea-worms were recovered from the following sites: deep fascia of right external abdominal muscles, fatty tissue covering right rectus, left chest wall (2), left rectus muscle, right eighth intercostal space, left leg just under the skin, left abdominal muscles, left ilio-inguinal region, right spermatic cord, left side of scrotum. From another dog 9 male and 23 female guinea-worms were recovered from the chest wall, subscapular and retro-oesophageal regions, the inguinal region and the extremities. One puppy which had received guinea-worm larvae by intravenous injection showed no guinea-worms in its tissues at necropsy.

Moorthy has published further observations on the development of *Dracunculus medinensis* larvae in cyclops. He finds that in hot weather (90–102° F) the first moult within the body cavity takes place between the fifth and seventh days, and the second between the eighth and twelfth days after infection of the cyclops, in cooler weather (55–70° F) the first occurs between the eighth and tenth days and the second between the thirteenth and sixteenth days. No further development beyond a slight increase in size was observed up to 107 days after infection. During the first 4 or 5 weeks the larvae move actively but subsequently remain quiescent, coiled in the body cavity of the cyclops. They do not show any tendency to escape from the cyclops while this remains active. The larvae become infective to the vertebrate host (the dog) in from 4 to 8 days after it has completely shed the exuviae of the second moult.

TREATMENT

Modern treatment*Phenothiazine*

Elliott records a new treatment by phenothiazine, the drug being given in doses of at least 1 gramme by deep intramuscular injection, the maximum effect is noted in from 5 to 7 days, when the process of extraction of the worm is carried out.

Elliott, M. (1942) *Trans R Soc trop Med Hyg*, **35**, 291

Moorthy, V. N. (1938) *Amer J Hyg*, **27**, 437

— and Sweet, W. C. (1938) *Amer J Hyg*, **27**, 301

HAEMATURIA

HAEMATURIA

Aetiology*Effect of sulphonamide treatment*

585

The introduction of the sulphonamide group of drugs has added a new cause of haematuria which is not uncommon. The haemorrhage is often very slight, and the accompanying presence of albumen in the urine, which may be the only change observed, may give rise to the suspicion of pyelitis, more especially as the drugs are given in acute infective conditions. Conditions in which the urine becomes more concentrated, such as hot weather, favour the occurrence of the haematuria. The presence in the urine of crystals of the drug which is being given and the prompt disappearance of the urinary changes on removal of the drug establish the diagnosis.

HAEMOGLOBINURIA

CLINICAL PICTURE

Haemoglobinuria due to chemical agents*Sulphonamide compounds*

589

Kohn recorded the case of a child, aged 1 year, with acute otitis media, who after 12 doses of 0.3 gramme each of sulphanilamide 3 times a day, developed haemoglobinuria which disappeared when the drug was discontinued. Strasser and Singer report another case in a patient 36 years old who was given prontosil rubrum for a sore throat occurring 7 days after appendicectomy. After 8 tablets had been taken

haemoglobinuria appeared, the prontosil was stopped and the haemoglobinuria disappeared in 3 days

Paroxysmal haemoglobinurias

Cold haemoglobinuria

Ascorbic acid—Pfeiffer and Arnove investigated on white rats the effect of vitamin C on paroxysmal haemoglobinuria produced by subcutaneous administration of glycerin, administration of ascorbic acid before the injection of glycerin raised the dose necessary to produce haemoglobinuria by 100 per cent or more. Armentano discovered C-hypovitaminosis in a patient with paroxysmal (cold) haemoglobinuria. After treatment for several days with 300 milligrams of ascorbic acid the haemoglobinuria disappeared. The protective action of ascorbic acid on red blood cells can be demonstrated *in vitro*.

592

Haemolytic anaemia with haemoglobinuria

Machiafava-Micheli type—Ham reported 3 cases of this syndrome. In 2 an increase in haemoglobinaemia occurred during sleep whether by day or by night, the third patient, whose spleen had been removed, did not show this feature. During sleep the pH of the blood falls, red cells are abnormally susceptible to haemolysis both *in vivo* and *in vitro* in plasma of increased acidity within a physiological range of pH variation. The oral administration of acid-forming salts increases the intravascular haemolysis, and vice versa.

In 2 further cases, with necropsies, recorded by Scott, Robb-Smith and Scowen, outstanding features were thrombosis of the central veins of the liver, siderosis of the renal tubules and erythroblastic hyperplasia of the bone marrow.

Paralytic haemoglobinuria (paroxysmal myoglobinuria)

Three further cases have been recorded. Huber, Florand, Lievre and Neret described a case of unknown aetiology in a child, aged 4 years, lasting a few days only and without any sequels, in the subsequent discussion, Debre recalled the 4 cases of this malady previously recorded: one in a child of 13 years, a second in a woman of 38, a third in a woman of 42 and a fourth in a child of 2½ years.

Armentano, L. (1936) *Nature, Lond.*, **137**, 910

Ham, T. H. (1937) *New Engl. J. Med.*, **217**, 915

Huber, J., Florand, J., Lièvre, J.-A., and Neret (1938) *Bull. Soc. med. Hôp. Paris*, **54**, 725

Kohn, S. E. (1937) *J. Amer. med. Ass.*, **109**, 1005

Pfeiffer, C., and Arnove, I. (1937) *Proc. Soc. exp. Biol., N.Y.*, **37**, 467

Scott, R. B., Robb-Smith, A. H. T., and Scowen, E. F. (1938) *Quart. J. Med.*, **7**, 95

Strasser, A., and Singer, K. (1938) *Med. Klinik*, **34**, 783

HAEMOPHILIA

Corrigendum

In the original article, Vol. VI, p. 129, in the paragraph with the title 'Use of egg-white', delete the last sentence beginning 'Sufficient time' and substitute by 'The lax records submitted by the authors are striking, but independent observers have not confirmed their claims'.

TREATMENT

Prophylaxis

Pohle and Taylor¹ state that globulin substance from citrated cellular-free beef plasma possesses properties similar to those of globulin prepared from normal human plasma, except for a slightly greater clot-accelerating property for haemophilic blood *in vitro*. Oral administration of beef globulin substance to adult haemophilic patients had not any effect on the coagulation time of the blood in the doses which were used in the authors' investigation.

The same workers also report² that, in haemophiles, repeated injections of lyophilized globulin substance, as well as normal globulin substance, produced a refractory period after the usual initial reduction in the coagulation time of the blood. Repeated injections of either normal plasma or of lyophil plasma into haemophiles maintained a reduced blood coagulation time without the development of a refractory phase, the refractory phase can be abolished at its height by a single injection of plasma. Both normal and lyophilized plasma probably contain substances which influence the reduction of the coagulation time of blood *in vivo* and which are not found in globulin substance preparations.

Lozner and Taylor observe that dialysis of cellular-free citrated normal human plasma yields a euglobulin precipitate with nearly all the clot-promoting activity of the plasma for haemophilic blood. Plasma euglobulin differs from acid-precipitated 'globulin substance' in possessing the ability of normal human plasma to maintain in haemophiles a reduced level of the coagulation time of blood when it is injected intravenously at 6-hourly intervals.

594

- Lozner, E L, and Taylor, F H L (1939) *J clin Invest*, **18**, 821
Pohle, F J, and Taylor, F H L (1938)¹ *J clin Invest*, **17**, 677
— — (1938)² *ibid*, **17**, 779

HAEMOPTYSIS

TREATMENT

- 595 Pollak and Cohen describe 3 principles in the treatment of haemoptysis (1) rest in bed with administration of codeine sulphate or phosphate $1\frac{1}{2}$ grains, (2) to try to secure local clotting by (a) cauterization or fulguration of a bleeding bronchial mass, and if this is not possible by (b) the use of drugs, the most effective of which are snake venom in increasing doses subcutaneously and a 1 per cent watery solution of Congo red given intravenously in doses of 10–15 cubic centimetres, the latter is said to increase the monocytes, blood platelets, and fibrinogen and thus decrease the blood clotting time, (3) to control the haemoptysis and treat the diseased lung at the same time by securing collapse of the lung This is done by artificial pneumothorax, phrenicectomy and thoracoplasty

Treatment of the attack

During 1941 no new drug was discovered, nor had any method been conceived which would control pulmonary haemorrhage in its most severe form Harrell and Ray appear to be amongst the first to try vitamin K They have used the synthetic 2-methyl-1, 4-naphthoquinone or thyloquinone in 7 cases of haemoptysis In addition bile salts have been given Not any beneficial effect was noticed The prothrombin time in 16 non-haemorrhagic cases was from 2 to 5 minutes and in 13 haemorrhagic cases it varied from 4 to 7 minutes Further investigations are being carried out

Sedatives

Schaffle states that the list of remedies shows our ineptitude Rest, absolute immobilization and judicious morphine medication remain still the best that can be done As a routine the author uses morphine, grain $\frac{1}{8}$, with atropine, grain $\frac{1}{30}$ – $\frac{1}{15}$, followed by 5 cubic centimetres of coagulen A small dose of atropine, such as grain $\frac{1}{160}$, is ineffective since it causes vasodilatation, whereas vasoconstriction follows larger doses

According to Schaffle, the latest entry in the field of therapy of haemoptysis is an extract of Shepherd's Purse containing the active principle of oxalic acid and related di-carboxylic acids, for intramuscular and intravenous administration In investigations made by his associate, Riesenbergl, the coagulation time is reduced to approximately from one-half to one-third of its normal value

Kaplan treated 8 pulmonary tuberculosis patients with haemoptysis by vitamin K given subcutaneously The dose was from 1 to 2 milligrams daily but some patients received as much as 4 milligrams for from one to 4 days The prothrombin determinations were done by the method of Howell before, during and after haemorrhage The prothrombin time showed only minor variations No effect on pulmonary bleeding in tuberculosis was observed

Harrell, C L, and Ray, A C (1941) *Virginia med Semi-Mon*, **68**, 451

Kaplan, R H (1941) *Med Bull Veterans' Adm, Wash*, **18**, 48

Pollak, B S, and Cohen, S (1940) *J med Soc N J*, **37**, 7

Schaffle, K (1941) *Sth Med Surg*, **103**, 245

HAEMORRHAGIC DISEASES

SYMPTOMATIC HAEMORRHAGIC STATES OR SECONDARY PURPURA

Aetiological factors

- 601 In a series of 500 cases of purpura Davis found 317 to be of symptomatic type The aetiological factors of importance were to be found in the following categories physical agents 7, chemical agents (gold, sulphapyridine) 5, bacterial disease 41, virus disease (measles) 1, spirochaetal disease 9, parasitic disease (trichiniasis) 2, cachexia 32, senility 67, scurvy 5, metabolic and endocrine disorders 17, dermatological affections 7, alimentary disturbances 3, cardiovascular diseases 49, chronic nephritis 7, rheumatism 46, blood diseases 18, neoplasm 1

Davis, E (1943) *Lancet*, **2**, 160

HAEMOTHORAX

AETIOLOGY

Dissecting aortic aneurysm

- 604 Post reports a case of haemothorax caused by leakage of a dissecting aortic aneurysm, such aneurysms often rupture into the pericardium but another common termination is the production of haemothorax, which develops more often on the left side than on the right Survival for more than a few days after pneumothorax caused by a leaking dissecting aneurysm does not seem to have been recorded

Post, F (1941) *Lancet*, **2**, 558

HAND, DISEASES AND DEFORMITIES
INJURIES

Complications

Division of tendons

Treatment—Tendon suture in the hand when the tendons are not enclosed in synovial sheaths as in the extensor tendons, with the exceptions of those over the back of the wrist, is sufficiently satisfactory to support the retention of the operation. Investigation of the final results, however, shows that so far as the flexor tendons are concerned, suture in their digital sheaths gives such bad results that some would recommend the immediate amputation of the digit when these tendons have been divided. Such unfavourable conclusions are possibly an overstatement, but there is no doubt that suture of flexor tendons in their digital sheaths is a disappointing operation. Nor are the reasons far to seek, for here the tendons of the flexor sublimis and profunda have a complicated arrangement, the one passing through the other, and they make a tight fit in their sheaths especially where the latter are reinforced over the levels of the interphalangeal joints. For obvious reasons the injury which severs the tendons almost always also divides the sheath, and thus the opening must be still further enlarged to allow of suture. In these circumstances the difficulties of suture are considerable, for practically all the methods at present in use necessitate some increased bulk of the tendon at the suture line even if the sutures are buried, and few methods give sufficient strength to make early movements safe. To achieve firm union requires some immobilization and this leads to adhesions of the tendons to one another and to the sheath. Such adhesions will be dense and not likely to respond to subsequent manipulation. In a really clean cut wound and in the absence of infection suture is probably worth a trial. Successful results are said to follow if the affected finger be held in complete flexion while the others are extended without any need for suture of the tendon, but satisfactory results from this method are rare.

614

Injuries produced by indelible pencils

A special type of lesion of the hand, commoner in the United States of America than in Great Britain for reasons connected with national custom, is that produced by the broken-off point of an indelible pencil. The dyes in this produce a local necrosis and a persistent wound. It is therefore necessary to excise the particle with a small amount of surrounding tissue which is coloured by the dye. These wounds are usually very superficial and easily dealt with once their character is recognized.

HEART DISEASES. I—CONGENITAL DISEASES

COURSE AND PROGNOSIS

Ash and Harshaw observed 230 cases of congenital heart disease in 14 years. Of these 102 patients had died, 73 per cent of deaths occurring in the first year of life. Of 94 school children 11 per cent died. The mortality rate in congenital heart disease largely depends upon the selection of patients, and the death rate in the cyanotic is twice as high as that in the acyanotic cases. Half the number of deaths were due to infections, of which pneumonia was the commonest, 40 per cent of the patients with cyanosis died of the lesion itself. The authors state that, whether cyanosis is present or absent, there is no indication for restriction of activity beyond the limiting capacity of the heart. These patients have not the handicap of continued infection which is present in the rheumatic patient, and functional capacity is often normal despite the marked physical signs. Other interesting facts adduced in this series were that there were 7 per cent of patients with mongolism, in 14.5 per cent there was mental retardation, and the question arises how far this was due to cerebral dysplasia or to a poor cerebral circulation, or to both. In 18 cases there were defects other than cerebral, and the total incidence of defects of all kinds was 35, or 10.9 per cent.

619

PATENT DUCTUS ARTERIOSUS

A patent ductus arteriosus is probably the third most common cardiac abnormality, and for some unexplained reason is more common in females. The ductus may remain patent as a sole abnormality, or as a compensation for some other gross departure from normal. When the ductus remains patent there is a shunt from the aorta to the pulmonary artery. The effects upon the heart and upon the individual are roughly directly proportional to the volume of blood shunted. Thus such signs and symptoms as dilatation of the pulmonary artery, vigorous pulsation in the neck, a low diastolic pressure and under-development are all traceable to this. Perhaps more important still is the risk of an infective endocarditis involving the abnormal structures, which occurred in 25 per cent of Abbott's autopsied cases. It may be observed that, in a personal series of 80 cases which have been examined by Brown at intervals for from 6 to 10 years (unpublished), only 4 have developed infective endocarditis.

628

Treatment

628

At the present time the possibility of ligature of the ductus arteriosus is attracting considerable attention. The attempt of Graybiel, Strieder and Boyer failed in the presence of an infective endocarditis, although the operation was successful. The first successful case may be credited to Gross and Hubbard in a girl aged 7 years who made an uneventful recovery. Gross described the operative technique employed in 4 cases. The incision is made in the third left intercostal space from the sternum to the mid-axillary line, and the rib above is divided at the costo-chondral junction. Incision of the pleura allows the left lung to collapse and facilitates the approach to the ductus through the mediastinal pleura. As regards the size of the ductus, the diameter matters little, the important factor is its length, the longer it is the more easily is it ligatured. The ligatures are applied, and sclerosing fluid is injected between them. Up to the end of 1940, 32 cases had been operated on, with a mortality of 7 per cent.

The indications for operation must be carefully considered. The best time for operation is in childhood before the second decade, and only those patients in whom the ductus is the sole abnormality should be chosen. Hubbard, Emerson and Green state that retardation of growth and development, peripheral signs of a large arterio-venous shunt (evidenced by a low diastolic pressure), and signs of cardiac insufficiency are the more important indications for operation. With closure of the ductus the diastolic pressure may be raised 30 millimetres.

DEFECTS OF THE INTERAURICULAR SEPTUM

629

Bedford, in a communication to the Cardiac Society of Great Britain and Ireland, described the clinical features of 53 cases of interauricular septal defect, 40 of which were in females. Mitral stenosis was also present in 8 cases. From a clinical standpoint these patients lead an active life until the late twenties, when symptoms and signs appear. These are breathlessness on exertion, and the late appearance of some cyanosis with minimal clubbing. The physical signs are those of dilatation of the pulmonary artery, and are a systolic thrill and diastolic shock over this area. A pulmonary systolic murmur is almost constantly present. A diastolic murmur due to pulmonary artery dilatation and incompetence was present in 10 of the cases. The X-ray picture shows gross enlargement of the heart to the left due to right ventricular hypertrophy. The pulmonary arc is grossly convex and prominent, and the right pulmonary artery is dilated and sometimes assumes aneurysmal proportions. The aortic knuckle is small and inconspicuous. The electrocardiogram commonly shows right-sided preponderance and in a few cases the axis is normal. The ventricular complexes may suggest a 'partial' bundle-branch block with inversion of the T wave in leads II and III. The general course is towards congestive failure, often with auricular fibrillation.

Ash, R., and Harshaw, E., Jun (1939) *Amer Heart J*, 18, 80

Bedford, D. E. (1940) Communication to the Cardiac Society of Great Britain and Ireland

Graybiel, A., Strieder, J. W., and Boyer, N. H. (1938) *Amer Heart J*, 15, 621

Gross, R. E. (1939) *New Engl J Med*, 220, 510

— and Hubbard, J. P. (1939) *J Amer med Ass*, 112, 729

Hubbard, J. P., Emerson, P. W., and Green, H. (1939) *New Engl J Med*, 221, 481

HEART DISEASES. II.—RHEUMATIC HEART DISEASE IN CHILDREN

COURSE AND PROGNOSIS

636

Mortality in boys

A survey of rheumatic carditis, which covered 200 patients, all boys, carried out during a period of 10 years was made by Cotton. There were 2 groups of children, and the observations were made in a special home reserved for boys suffering from the disease. In the first group the average stay was 4½ months, in the second group it was 6 months. When after 10 years of observation the figures were investigated, the boys of the first group showed a survival rate of 54 per cent, 40 per cent were dead for certain but trace had been lost of 6 per cent. In the second group there were 49 per cent alive, 34 per cent dead for certain and 17 per cent untraceable. There were 21 deaths in the first 5 years and 18 deaths in the second 5 years. Taking the statistics all over, mitral stenosis had a bigger death rate than had mitral regurgitation, but the most dangerous of all was a combination of aortic regurgitation and mitral stenosis, for half the number of patients died. Enlargement of the heart necessarily meant that the prognosis would be worse than in those in whom there was little or no enlargement. A careful assessment of the structural damage of the heart fabric and a constant review of the physical signs of activity of rheumatic disease are fundamentals in coming to a decision with regard to prognosis and treatment. A close watch of the temperature and pulse and a frequent taking of the erythrocyte sedimentation rate

provide the criteria of rheumatic activity. Furthermore, a child with rheumatic carditis should be weighed at regular intervals, for a loss of weight or a stationary reading is sure evidence that the disease is not under control. It is very difficult to evaluate the heart signs, which are not always of the greatest help in reaching an estimate of the patient's condition. One active sign which may remain for months is partial heart block, which the electrocardiogram registers by a lengthening of the P-R interval. This phenomenon is common and may for many months be the one remaining sign of acute infection. If auricular fibrillation persists, the prognosis must be a bad one, for statistics show that in most of these cases the patient dies within 3 years.

Cotton, T. F. (1942) *Brit med J*, 2, 473

HEART DISEASES. IV—MYOCARDIUM DISEASES MYOCARDITIS

Pyæmic and septicaemic forms

Bang describes 6 cases which he believes were examples of gonococcal myocarditis. The cases occurred in the course of acute or chronic complicated gonococcal infection. The chief complication was arthritis and the diagnosis rested finally on electrocardiographic changes which were demonstrated in each patient. Bang suggests that the condition may be commoner than is generally supposed, and that a routine gonococcal complement fixation test in so-called rheumatic arthritis cases would assist in its discovery.

Bang, O. (1940) *Brit med J*, 1, 117

HEART DISEASES. VI—ENDOCARDITIS, MALIGNANT SUBACUTE BACTERIAL ENDOCARDITIS

Treatment

The relative immunity of *Streptococcus viridans* to attack by leucocytes and anti-bacterial substances may depend upon the shelter given to it by an accumulation of platelet thrombus which forms the characteristic vegetations in this condition. If this progressive deposit of platelets could be prevented, it is reasonable to conjecture that leucocytes, natural immune bodies and chemotherapeutic substances might then reach the organisms in effective concentration. Since Murray and his co-workers showed that heparin prevented the formation of platelet thrombus in dogs, it may be assumed that it can prevent the increase in size of the vegetations forming in subacute bacterial endocarditis in man. Kelson and White treated 7 patients with this disease with heparin and sulphapyridine. Heparin in a strength of 2,000 units per 100 cubic centimetres of physiological saline was administered by continuous drip at a rate of from 15 to 20 drops per minute for 14 days. Sulphapyridine (4 to 6 grammes daily) was given for a week before and during and for a week after the infusion of heparin. Two of the 7 patients had reactions from impure heparin and the treatment had to be abandoned, 2 patients died from the disease within a few days, the remaining 3 patients were free from all symptoms and had negative blood cultures 19, 18 and 4 weeks respectively after discontinuing treatment. Friedman and his co-workers have also advocated the use of heparin in subacute bacterial endocarditis.

It is estimated that about one-fifth of all patients with patent ductus arteriosus develop subacute bacterial endocarditis. This fact alone allocates great importance to the surgical procedure of closing the ductus as described by Gross (see p. 120). It is likely that closure will prevent the onset of bacterial endocarditis, and even when this complication has already ensued, in view of the serious prognosis resort to surgery is justified in the hope that it might improve the outlook in early cases.

Heyer and Hick have collected 31 cases of subacute bacterial endocarditis in which cures were effected by sulphonamide treatment, including 5 cases which were associated with congenital heart disease.

Friedman, M., Hamburger, W. W., and Katz, L. N. (1939) *J Amer med Ass*, 113, 1702

Gross, R. E. (1939) *Ann Surg*, 110, 321

Heyer, H. E., and Hick, F. K. (1941) *Ann intern Med*, 15, 291

Kelson, S. R., and White, P. D. (1939) *J Amer med Ass*, 113, 1700

Murray, D. W. G., Jaques, L. B., Perrett, T. S., and Best, C. H. (1937) *Surgery*, 2, 163

HEART DISEASES: VII.—MITRAL VALVE DISEASES MITRAL STENOSIS

Clinical picture

Relative mitral stenosis

The term, relative mitral stenosis, has been adopted by Bramwell in order to describe the effects of increased flow of blood through a normal mitral valve. Bramwell considers that the duplication of the second heart sound at the apex—generally

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regarded as a sign of organic mitral disease—is physiological. The younger the patient the commoner the duplicate second sound. Less than 19 per cent out of a group of 835 recruits showed this sign and it was present in 43 per cent of those under 20 years of age and in only 10 per cent over the age of 20. Bramwell emphasizes that most of the young men concerned seemed to be in perfect health (70 per cent in Grade 1). The X-ray film showed that the pulmonary arch was more prominent in those who had duplication of the second sound. The apical systolic murmur or impurity of the first sound at the apex is a sign associated with mitral disease and with the duplication of the second sound. The murmur is explained as being caused by a mitral incompetence in which the ventricles are so over-filled that the mitral valve acts as a sort of safety valve. This would explain the so-called presystolic murmur which is sometimes heard in athletes.

Bramwell, C (1943) *Brit Heart J*, 5, 24

HEART DISEASES IX.—RIGHT SIDE DISEASES

HYPERTROPHY

Diagnosis

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According to Wood and Selzer the tall spiked P wave in the electrocardiogram, which is generally associated with tricuspid stenosis, congenital pulmonary stenosis, and cor pulmonale, may indicate hypertrophy of the right auricle.

Brill and Krygier review 20 cases of primary pulmonary vascular sclerosis, and state that the diagnosis of the condition depends upon the following factors: (1) The demonstration (especially by roentgenographical and electrocardiographical means) of the existence of pronounced strain of the right but not of the left ventricle, and (2) the exclusion by every available means of all other known causes of right ventricular strain, especially chronic pulmonary disease, mitral stenosis and congenital heart disease. The authors suggest that obliterative vascular disease bears a direct aetiological relation to the accompanying changes in the right side of the heart and to the resultant clinical manifestations. The hypothesis is put forward that primary pulmonary vascular sclerosis is a physio-pathological response to pulmonary hypertension of unknown origin, perhaps analogous to essential systemic hypertension.

Cor pulmonale

Clinical picture

In describing the clinical manifestations of the various types of right-sided heart failure Brill uses the term cor pulmonale to embrace all forms of cardiac strain and failure in which the right side of the heart is involved either as an initial circulatory disorder or as a consequence of an antecedent failure of the left side of the heart (secondary cor pulmonale), and he considers that in the large majority of cases the immediate cause of the condition is an increased resistance to the blood flow in the lesser circuit at any point between the pulmonary conus and the mitral valve.

The author groups the general symptoms and signs of cor pulmonale as follows:

(1) Manifestations of the underlying cardio-pulmonary disease: breathlessness, cyanosis, polycythaemia, haemoptysis, clubbing of the fingers and toes, together with specific signs of some such chronic pulmonary condition as emphysema, tuberculosis and bronchiectasis.

(2) Disturbances arising directly from strain and failure of the right heart chambers: (a) an increased venous pressure in the venae cavae, engorgement of the superficial veins, subcutaneous oedema, visceral congestion, serous effusions, oliguria with albuminuria and haematuria, and an increased cerebrospinal pressure, (b) hypertrophy and dilatation of the right auricle, the right ventricle, and the pulmonary conus and dilatation of the pulmonary artery, (c) accentuation of the second sound at the pulmonary base, exaggerated pulsation, murmurs, and thrills in the second and third interspaces on the left side and possibly gallop rhythm at the apex region.

For descriptive purposes Brill divides primary cor pulmonale into 3 well defined groups—the acute, the subacute and the chronic forms of the disease.

Acute cor pulmonale—This condition is caused by sudden obstruction of the trunk or the first branches of the pulmonary artery by an embolism or by rapid thrombosis, the onset of the condition is explosive—suffocating breathlessness, severe pain in the chest, cyanosis, profound shock, a fast pulse, a low blood pressure, gallop rhythm, pericardial friction at the base, fever, leucocytosis, and varying degrees of dilatation of the pulmonary artery and conus which may be demonstrable by palpation, percussion and X-ray examination, the following cardiographic changes were regarded by McGinn and White as characteristic of acute cor pulmonale: 'The presence of a Q wave and late inversion of the T wave in Lead III, the rather low origin of the T wave with a gradual staircase ascent of the ST interval in Lead II, and a prominent S wave with a slightly low origin of the T wave in Lead I.'

Wood analyses 10 cases of acute cor pulmonale secondary to pulmonary embolism, and emphasizes the value of chest lead electrocardiography in the diagnosis of the condition. He states that, in pulmonary embolism sufficient to cause right ventricular stress, there is sharp inversion of the T wave, maximal and for the longest duration in the right pectoral lead, usually, but for a shorter duration, in the left pectoral lead, and rarely, and for the shortest duration, in lead IV. He points out that similar changes may be found in all conditions giving rise to right ventricular stress and that multiple chest lead cardiograms afford a good method of differential diagnosis in the somewhat similar conditions of acute pulmonary embolism and posterior myocardial infarction.

Subacute cor pulmonale—Subacute cor pulmonale is characterized by the rapid development of signs and symptoms of right ventricular strain in a patient who gives no history of antecedent cardio-pulmonary disease or any other condition known to be capable of producing strain of the right side of the heart.

The condition occurs in relatively young subjects, from 36 to 40 years of age, the cause being a rapidly progressive stenosis of the pulmonary vascular circuit by metastatic carcinomatous invasion of the pulmonary lymphatics and arterioles, a scirrhous carcinoma of the stomach being the primary lesion in the majority of the cases that have so far been recorded.

The presenting symptoms are breathlessness and an unproductive cough, both of which rapidly increase in severity, to terminate fatally with signs of acute right heart failure.

Mason records a case of subacute cor pulmonale secondary to embolic vascular obstruction by carcinoma cells arising from primary carcinoma of the breast, and reference is made to additional cases in the literature.

Chronic cor pulmonale—The aetiological factors of chronic primary cor pulmonale include mitral stenosis, pulmonary fibrosis resulting from pneumoconiosis, tuberculosis or other chronic infections, emphysema secondary to asthma, chronic bronchitis or other pulmonary disease, and, less often, deformity of the chest (kypho-scoliosis), congenital heart disease and primary pulmonary arteriosclerosis.

The incidence of chronic cor pulmonale, which implies right ventricular hypertrophy with congestive failure secondary to chronic pulmonary disease, was investigated by Griggs and his colleagues. They reviewed the protocols of all the chronic pulmonary lesions in 18,000 autopsies at Los Angeles County Hospital and their findings are summarized in the accompanying table.

	TOTAL CASES	CASES SHOWING RIGHT VENTRICULAR HYPERTROPHY	CASES SHOWING EVIDENCE OF CONGESTIVE FAILURE
Chronic bronchitis	92	0	0
Chronic pulmonary tuberculosis	— 1470	3 7%	1 8%
Bronchiectasis	— 68	8 8%	4 4%
Emphysema	— 45	28 9%	22 3%
Pneumoconiosis	— 24	54 2%	50%

The clinical findings prior to the onset of cardiac failure include as a rule certain characteristic signs in the lungs together with X-ray evidence of enlargement of the right ventricle and pulmonary conus and varying degrees of dilatation of the pulmonary arteries, cases of long standing may develop an extreme, almost black, cyanosis with cerebral symptoms (headache, mental confusion and somnolence) and attacks of anginal pain (hypercyanotic angina), this syndrome, at times referred to as Ayerza's disease, is a possible development in those cases of chronic cor pulmonale which happen to involve extensive pulmonary arteriosclerosis with hypertension and narrowing of the pulmonary vascular bed.

The course of chronic primary cor pulmonale is, as a rule, slowly progressive over a period of years, and although a certain number of patients die of congestive heart failure or acute circulatory collapse, the majority succumb to intercurrent infections.

Secondary cor pulmonale—Secondary cor pulmonale represents the advanced stage of general heart failure, its immediate cause being pulmonary congestion and increased resistance in the pulmonary circuit resulting from antecedent decompensation of the left ventricle, the remote causes of secondary cor pulmonale are therefore such conditions as hypertensive heart disease, deformities of the aortic valve, and coronary artery disease, all of which induce strain and ultimate failure of the left ventricle.

More often than not the onset of left ventricular failure is rapidly (hours, days or weeks) followed by right-sided decompensation, but on the other hand in hypertensive conditions and in some cases of aortic disease left ventricular failure is in evidence for an extended period before there are any obvious signs of embarrassment of the right heart, it happens moreover not infrequently that the onset of right heart failure (peripheral oedema, congestion of the liver and distension of the

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superficial veins) may relieve for a time the pulmonary congestion, also incidentally the breathlessness and the attacks of paroxysmal dyspnoea secondary thereto

Parker reports observations based on an anatomical study of the heart and the pulmonary arterial tree in 32 cases of emphysema. He found that emphysema produced enlargement of the right ventricle in 75 per cent and cardiac failure with decompensation in 44 per cent of the entire group, and concluded that the severity of emphysema was closely correlated with the incidence of congestive heart failure as well as with the frequency and extent of right ventricular enlargement

Arteriosclerosis of the pulmonary tree was present in 80 per cent and these changes apparently represented secondary manifestations of hypertension in the pulmonary circuit

Diagnosis

Scott and Garvin regarded the clinical recognition of cor pulmonale prior to the development of congestive failure as a difficult problem, such presenting symptoms as cough, dyspnoea on exertion, cyanosis and poor exercise tolerance being possibly entirely accounted for by the pulmonary disability, furthermore they were of opinion that in patients at or beyond middle life it was impossible to evaluate the influence of such complicating factors as hypertension and coronary artery disease, for these reasons they suggested that conclusions regarding the incidence of chronic cor pulmonale must depend for their validity upon evidence afforded by necropsy findings, as, moreover, no method is yet available for measuring the pulmonary blood pressure they considered that the only reliable index of right heart strain was hypertrophy or dilatation of the right ventricle, their criterion in this respect being a ventricular wall of 5 millimetres or more in thickness, they investigated a series of 41 cases of cor pulmonale associated with advanced lung disease and it is noteworthy that their series excluded cases of hypertrophy of the right heart due to mitral disease, also all cases of aortic disease, hypertension and coronary atheroma, of the 41 cases 70 per cent were admitted to hospital with congestive heart failure, the short duration and rapid progress of which were emphasized by the high mortality rate, 84 per cent of the whole series having succumbed within a few months of their first cardiac breakdown. The authors concluded as follows 'Observations made in this series of cases entirely support the conclusions of older clinicians and pathologists regarding the relation between chronic emphysema and failure of the right side of the heart, the clinical course and the autopsy findings indicate that the right ventricle is burdened in emphysema, presumably by an elevation in pulmonary pressure, and that it undergoes dilatation and hypertrophy and ultimately fails'

Cardiogram

The cardiogram in cor pulmonale was investigated by Comeau and White, their conclusion being that the condition is invariably associated with some degree of right axis deviation, they stated further that, in cases of transversely placed or enlarged hearts, right axis deviation is almost always due to a cardiac defect which has led, either primarily or secondarily, to right ventricular strain

The possible development of right ventricular hypertrophy as the result of left ventricular failure was recognized by Thompson and White, who suggested that, in such circumstances, axis deviation to the left is in part or wholly counter-balanced or that the cardiogram may show the changes characteristic of axis deviation to the right

VALVULAR DISEASE

Pulmonary stenosis

Stenosis of pulmonary valve due to atheroma

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Doniger reports the case of a man, aged 64, who died of carcinoma of the pancreas and in whom there had been no clinical features of cardiac or pulmonary impairment

The necropsy findings included hypertrophy and dilatation of both ventricles, the coronary vessels were tortuous and rigid from extensive atheroma, there was slight atheroma of the aortic and the mitral valves with calcification of the aortic ring, all three pulmonary cusps were greatly thickened but not fused, the central portions bulging upwards into the pulmonary artery, the valve orifice was narrowed to about half the normal width

Tricuspid stenosis

Clinical picture

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Cooke and White divide cases of tricuspid stenosis into 2 groups (1) young patients in the first 3 decades who die of rheumatic fever and (2) older patients in whom mechanical factors induced by cardiac lesions play an important part

The older group is characterized by a relatively long survival after the appearance of congestive symptoms and signs indicative in most other circulatory disorders of death in the near future. The diagnosis is difficult and due attention to the history, clinical examination of patient and X-ray examination of the heart is of fundamental importance. No one sign is pathognomonic but clues in order of importance are listed as follows. A mid-diastolic murmur localized over the tricuspid area, chronic

and accentuated systolic pulsation of the deep jugular veins, ascites in the absence of lung congestion, enlargement of the heart shadow to the right, deviation of the oesophagus to the left, cyanosis and sometimes jaundice, an enlarged liver with or without pulsation, a persistently raised venous pressure and a prolonged right heart circulation time

- Brill, I C (1939) *Ann intern Med*, **13**, 513
 — and Krygier, J J (1941) *Arch intern Med*, **68**, 560
 Comeau, W J, and White, P D (1939) *Amer Heart J*, **18**, 334
 Cooke, W T, and White, P D (1941) *Brit Heart J*, **3**, 147
 Doniger, C R (1939) *J Path Bact*, **48**, 472
 Griggs, D E, Coggin, C B, and Evans, N (1939) *Amer Heart J*, **17**, 681
 McGinn, S, and White, P D (1935) *J Amer med Ass*, **104**, 1473
 Mason, D G (1940) *Arch intern Med*, **66**, 1221
 Parker, R L (1940) *Ann intern Med*, **14**, 795
 Scott, R W, and Garvin, C F (1939) *Trans Ass Amer Phys*, **54**, 172
 Thompson, W P, and White, P D (1936) *Amer Heart J*, **12**, 641
 Wood, P (1941) *Brit Heart J*, **3**, 21
 — and Selzer, A (1939) *Brit Heart J*, **1**, 81

HEART DISEASES. X.—HEART FAILURE

CLINICAL TYPES

Congestive heart failure

Aetiology

Congestive heart failure with normal rhythm is not uncommon in rheumatic heart disease complicated by pregnancy (Bramwell and Longson)

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Signs of ventricular failure

Acute failure of both right and left ventricles is seen in vitamin B₁ deficiency due to chronic alcoholism (Jones and Bramwell)

Right ventricular failure

The problem of right ventricular failure has recently attracted considerable attention. The clinical picture is characteristic, with intense venous engorgement, oedema and ascites, dyspnoea is conspicuous by its absence but cyanosis may be marked. This type of failure may be the result of chronic pulmonary disease or of sclerotic changes in the pulmonary vessels, but in some cases neither of these factors is present and it has been suggested that the syndrome results from hypertension in the pulmonary circuit during life.

TREATMENT

Drugs

Digitalis

Gavey and Parkinson, in a recent investigation, showed that digitalis is useful in the treatment of heart failure with normal rhythm. In fact, if cases of auricular fibrillation due to rheumatic heart disease are excluded, digitalis gives equally good results in normal rhythm and in auricular fibrillation.

Administration in single doses—Digitoxin may be given if it is desired to give digitalis in single doses. It is recommended that a single dose of 1.26 milligrams be given in the average case. Less than 5 per cent of patients have toxic sequelae, the latter take the form chiefly of gastro-intestinal irritation.

Mercurial diuretics

Evans and Paxon submitted the following mercurial diuretics to a clinical trial on 50 patients with heart failure: salyrgan, mersalyl, neptal, esidrone, novurit. The object was to decide their relative diuretic potency. The best method of administering them was also investigated as well as the best means of augmenting their natural diuretic action. The results of this investigation were as follows: (1) neptal and esidrone when given intravenously or intramuscularly produced the largest diuresis, rather larger than salyrgan and much larger than mersalyl, (2) the intravenous method almost always produced greater diuresis than the intramuscular method, (3) of the two rectal suppositories tried, novurit gave much better results than salyrgan, (4) neptal tablets by mouth proved much more efficient than mersalyl tablets, salyrgan tablets, or novurit suppositories, ammonium chloride was always given in association, (5) although the urinary output after oral administration of a mercurial salt was greatest when 0.48 gramme of neptal was used, satisfactory diuresis was also produced by 0.32 gramme, (6) 30 grains of ammonium chloride given 2 hours before the administration of a mercurial preparation proved to be the best form of premedication. Enteric chocolate-coated tablets each containing 7.5 grains proved the most convenient form of dispensing ammonium chloride, (7) in a patient confined to bed with heart failure, and especially

with oedema, standard treatment would include the injection of a mercury diuretic (2 cubic centimetres) intravenously or intramuscularly every third day, preceded on each occasion by the administration of 4 tablets of ammonium chloride by mouth 2 hours before. During the ambulatory stage the patient should take neptal tablets (3 in all or 0.48 gramme) twice weekly in the more severe case and once a week in the less severe case, after the same premedication, and should receive an intravenous or intramuscular injection (2 cubic centimetres) at intervals according to need.

Surgical measures

Thyroidectomy

Cutler and Hoerr report a continued investigation for 5 years of 57 cases of total thyroidectomy for heart disease. Most of the patients had not been relieved by medical treatment, and presented a serious operative risk. In 32 cases with angina pectoris there were 12 survivors and in 25 with congestive failure there were 4. There were 5 post-operative deaths. The best results were obtained in patients with angina pectoris, 26 of the 27 patients who survived for more than 6 months being relieved of pain for 6 months or longer and 8 of the 12 five-year survivors having been relieved. The authors conclude that in selected cases of intractable angina pectoris total thyroidectomy is worthy of trial.

Bramwell, C., and Longson, E. A. (1938) *Heart Disease and Pregnancy*
London

Cutler, E. C., and Hoerr, S. O. (1941) *Ann Surg.* **113**, 245

Evans, W., and Paxon, T. (1941) *Brit Heart J.* **3**, 112

Gavey, C. J., and Parkinson, J. (1939) *Brit Heart J.* **1**, 27

Jones, A. M., and Bramwell, C. (1939) *Brit Heart J.* **1**, 187

HEAT-STROKE AND HEAT-EXHAUSTION

AETIOLOGY

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With the object of elucidating the effects of high temperature Marsh experimented in Iran on hares and rabbits, which do not perspire, and concluded that in rabbits in a very hot environment a rise of temperature is inevitable, that, when a high brain temperature is reached, the prognosis depends upon its duration, and therefore in all cases of hyperthermia reduction of the temperature should be effected as an emergency measure, and that acclimatization plays a large part in the ability to withstand high temperatures. His paper emphasized the importance of anoxaemia and circulatory failure, factors which are confirmed by Kopp and Solomon.

During 1938 and 1939 Marsh carried out experiments on heatstroke (unpublished) in Iran, assisted and financed by the generosity of Lord Cadman. He induced experimentally severe heatstroke in rabbits and found that after apparent recovery, sometimes many hours later, a condition occurred which was characterized by falling blood pressure, rising heart rate, rising haemoglobin values and falling body temperature. In one case the circulatory condition responded favourably to subcutaneous injection of cortin (adrenal cortex preparation) given in large doses. This condition conforms to the definition of shock given by Moon, namely 'Shock is a circulatory deficiency neither cardiac nor vasomotor in origin, characterized by decreased blood volume, decreased cardiac output (reduced volume flow) and by increased concentration of the blood'. It appeared that the deciding factor in the type of shock observed was uncontrollable dilatation of the intramural pores of the capillaries. This was well shown in the splanchnic area, where, on examination of a rabbit with very high haemoglobin values (140 per cent) much free clear fluid was constantly found in the abdominal, pleural and pericardial cavities. Intense spasm of small arterioles in all parts of the body was also constantly associated with this state of shock, apparently a reparative effort. A number of the experimental animals, examined immediately after death from heatstroke, showed microscopic lesions scattered sparsely or profusely in the cerebrum, midbrain and cerebellum. Quite often one or more of these lesions involved the hypothalamic region of the brain. Lesions of the brain found on microscopic examination after death from heatstroke or from induced hyperthermia have been described by Hartman and other authors. All these descriptions, however, are of haemorrhagic lesions, the peculiarity of the lesions in the rabbit was their apparently ischaemic nature.

PATHOLOGY AND MORBID ANATOMY

Blood chemistry

Chakravarti and Tyagi analysed the chemical and physical changes in the blood and urine of 10 patients suffering from 'effects of heat', and correlated them with the meteorological data. They found a tendency to retention of non-protein nitrogen, and other indications of renal insufficiency, the loss of chlorides in the sweat was not estimated, as it is stated that sweating is not a feature of heatstroke, although this is difficult to explain, they found the blood chlorides to be reduced in spite of low urinary chloride, the blood lactic acid and other anions were increased.

HEAT-STROKE—HEMIATROPHY AND HEMIHYPERTROPHY

Gibson and Kopp found that in artificially induced fever there is a diminution in the volume of the circulating blood caused by loss from the skin and lungs. The volume cannot be restored by oral ingestion of fluids, but can be maintained at the pre-febrile level by intravenous administration.

Further experiments on rabbits

Heatstroke

Heatstroke and heat exhaustion are still very prevalent among members of the Forces in the Middle East in spite of the considerable advance in the knowledge of this disorder, which had been generally accepted long before the beginning of the present war. Marsh has carried out further (unpublished) experiments on the condition of hyperthermia in rabbits. With a specially constructed Cambridge electrocardiograph semicontinuous records of the heart's responses were made on 24 rabbits before, during and after the experimental production of hyperthermia by exposure to the summer sun. After the peak of hyperthermia, 112° F or more in all cases, cooling treatment was immediately begun and the electrocardiographic records continued. Except in 4 rabbits that died at or just after the peak of temperature, no significant changes in the electrocardiogram were observed in any of the animals. These observations confirm previous work on the condition of animals and man during and just after extreme degrees of hyperthermia. It is clear that the circulatory failure which is so evident a feature of many of these cases is peripheral and not central in origin. In other words the condition known as shock rather than that of heart failure is the explanation in most cases of the severe symptoms observed. One of the experimental rabbits had a rectal injection of 3.5 cubic centimetres of absolute ethyl alcohol in 10 cubic centimetres of distilled water half an hour before the experiment. This animal went blue and died at the peak of body temperature—112° F—but the electrocardiographic changes were not significant. The alcohol merely intensified the severity of the peripheral circulatory failure, or shock, in clinical terms.

CLINICAL PICTURE

McCance suggests that the difference between individuals in their tolerance of hot climates may be associated with individual differences in the amount of sodium chloride lost in the sweat. In a series of laboratory experiments on human subjects he found that some subjects cannot be rendered deficient in chloride by repeated sweats because after a time almost no sodium chloride is excreted, some, on the other hand, continue to lose considerable amounts and would be likely to suffer in a hot climate unless an adequate intake of sodium chloride was provided.

Further information on physiological studies of high temperature conditions are given by Dill. The statement in Vol. VI, p. 405, that air-conditioning is not practised in the Witwatersrand gold mines is incorrect.

TREATMENT

Curative

Convulsions

In the treatment of convulsions in cases of human heatstroke the administration of oxygen by a face-mask—Cowan and Mitchell type preferred—in addition to treatment by cooling is often effective even in patients who have had a temperature of 109° F with unconsciousness for some hours. Venesection is often ineffective since the blood is like toothpaste through superdehydration. The giving of intravenous cool saline is helpful. Mechanically cooled rooms for treatment are essential.

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Dill, D. B. (1938) *Life, Heat, and Altitude, Physiological Effects of Hot Climates and Great Heights*. London.

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Hartman, F. W. (1937) *J. Amer. med. Ass.*, **109**, 2116.

Kopp, I., and Solomon, H. C. (1937) *Arch. intern. Med.*, **60**, 597.

McCance, R. A. (1938) *Lancet*, **2**, 190.

Marsh, F. (1938) *Trans. R. Soc. trop. Med. Hyg.*, **32**, 371.

HEMIATROPHY AND HEMIHYPERTROPHY

ACQUIRED HEMIATROPHY

Partial hemiatrophy (Parry-Romberg's syndrome)

Effect of cerebral scars

Apart from lesions of the spinal cord occurring in infancy and large injuries of a hemisphere of the brain, a positive factor in acquired hemiatrophy may be a lesion of the cerebral cortex alone. Penfield and Robertson in a study of 32 cases in which

CUMULATIVE SUPPLEMENT 1945

the outstanding sign was the occurrence of epileptic fits investigated lesions of the excitomotor area of the brain in order to establish the relation of these lesions to hemiatrophy. They came to the conclusion that infantile lesions of the post-central gyrus limit the growth of the contralateral part of the body almost invariably, the thorax and face being involved usually, lesions elsewhere of the cortex did not produce such changes. It is pointed out that contralateral hypertrophy of the body is not produced by lesions of the cortex.

Penfield, W., and Robertson, J. S. M. (1943) *Arch Neurol Psychiat*, Chicago, 50, 405

HERNIA

EXTERNAL ABDOMINAL HERNIA

Treatment

General treatment of hernia

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Post-operative treatment and prognosis—Douglas analyses 103 cases of strangulated external abdominal hernia which were treated by surgical operation, with a mortality of 16.9 per cent. The significant factors in the mortality were the age of the patient and the duration of strangulation. The post-operative management of aged patients is discussed.

Types of hernia

Inguinal hernia

Robins explains the mechanism of recurrence, and its prevention, he points out that the construction of a new inguinal canal cannot possibly cure direct hernia, because this type occurs at the lower end of the inguinal canal and is due to muscular deficiency. Recurrence of the hernia after operation is due to the presence of an aperture which is difficult to obliterate. By making use of the ligamentous covering of the superior surface of the pubic bone and by using the fascial suture recommended by McArthur, obliteration of the aperture may be achieved.

Filigree operation—Cole discusses and defends the filigree operation for inguinal hernia, and states that this method has been successfully employed at the Seamen's Hospital, Greenwich, for many years and that the results justify its continuation, the author points out that recent evidence confirms that the use of fascia has not fulfilled its early promise.

Cole, P. P. (1941) *Brit J Surg*, 29, 168

Douglas, D. M. (1942) *Brit med J*, 1, 354

McArthur, L. L. (1904) *J Amer med Ass*, 43, 1039

Robins, C. R. (1941) *Ann Surg*, 114, 118

HERPES

HERPES SIMPLEX

Aetiology

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Since it has been proved that 70 per cent of normal persons carry the virus of herpes simplex the occurrence of eruptions is to be expected in a certain number of individuals. The aphthous stomatitis of the infant is an early sign of herpes and the virus is known to take refuge in the mucous membrane or in a sensory ganglion and to remain there for years, in these circumstances it displays its antagonism to its host from time to time by setting up lesions of the skin. The 'trigger' may be an infection or gastric disturbance or a state of hormone imbalance. It is fewer however that is the most common factor in the production of herpes simplex. It must be remembered too that recurrent herpes may result from local conditions such as sunburn or a septic focus, it may occur with regularity immediately before a menstrual period.

Treatment

So far there is not any specific remedy, Hruszek's method not having been proved successful in hands other than his own. Herpes vaccine as advocated by Brain has had some success especially when erythema multiforme was co-existent. Nicotinic acid therapy has been of value in certain cases—it seems to stimulate the recovery of the skin. The sulphonamides are not of any use. Locally a mixture of 2 per cent of phenol in calamine lotion is most satisfactory for the lesions.

Brain, R. T. (1936) *Brit J Derm*, 48, 21

Hruszek, H. (1933) *Derm Z*, 68, 27

HODGKIN'S DISEASE

COURSE AND PROGNOSIS

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Baker and Mann analysed 65 cases of Hodgkin's disease seen at Guy's Hospital, London, between October 1926 and October 1937, all but one of which were confirmed either by biopsy or by necropsy. Of the 65 cases 47 were males and 18 females, the ages were between 7 and 67 years, the maximum incidence being in the second and third decades. Half the number of patients died within 2 years of the occurrence of the first symptoms, the extremes in this duration being one month and 17 years, and the average expectation of life being estimated at 18 months. In all but 4 cases

the superficial lymphatic glands were involved and in all but 3 cases from the onset. In 54, or 83 per cent, the cervical lymphatic glands were affected. Hodgkin's disease very rarely occurred primarily in the lungs, the involvement being nearly always secondary to disease of the mediastinal glands. The following classification was suggested: (1) The involved mediastinal glands compressing or even causing collapse of the lungs without infiltrating them, this was usually bilateral, but when unilateral the right side was generally affected. (2) Lung involvement: (a) diffuse peribronchial spread, (b) massive lung involvement, and (c) discrete nodular involvement. (3) Pleural involvement: (a) deposits in the pleura, in 3 cases, found after death, (b) with effusion, in 3 cases. Lung involvement occurred in 30 cases, in 5 of which the mediastinal glands were not affected. The spleen was clinically enlarged in 35 and the liver in 20 cases. In none of the 65 cases were lesions of the alimentary tract apparent. There were 8 cases of disease of the central nervous system, 2 being fatal from paraplegia, one of them after laminectomy which showed epidural masses of lymphadenoma. The blood showed a polymorphonuclear leucocytosis (more than 8,400 polymorphonuclears per cubic millimetre) in 16 cases, or 28 per cent, and a leucopenia (less than 3,000 leucocytes per cubic millimetre) on 4 occasions only. Eosinophilia (5 per cent or more) was noted in 11, or 20 per cent, of the cases. In 23 cases, or 41 per cent, the haemoglobin was at some time during the course of the disease below 60 per cent. In all cases in which the disease is clearly limited to peripheral and accessible glands surgical removal, followed by regular X-ray exposures, is advocated. Of 4 cases so treated 2 were stated to be cured.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The main diagnostic elements

The characteristic histological features of the lymphatic gland of Hodgkin's disease are widespread fine fibrosis, presence of polymorphonuclear cells and occasionally of eosinophil cells. The diagnosis cannot be certain unless a biopsy has been done and it should be remembered that the most advanced changes in the structure of the gland are to be found in the earliest involved lymphatic glands, this should influence the selection of a typical gland for biopsy. Gordon's test is still the most useful test known. In addition to the reaction obtained when intracerebral inoculation of gland suspension is made in rabbits or guinea-pigs, there are changes in the leucocyte count of the blood, the leucocytes may be of reduced, of normal, or of very much increased amount, a leucocytosis of 30,000 being known. The differential count shows that the polymorphonuclear cell predominates, often the proportion may be 70 per cent and it may be as high as 90 per cent. There is also a high erythrocyte sedimentation rate, early in the disease the readings may be normal but soon the rate advances and ultimately a very high erythrocyte sedimentation rate may be discovered although the patient may not be particularly anaemic or ill. It is almost certain that the lesions of Hodgkin's disease represent a response on the part of the lymphatic glands to some infective agent.

Gordon's test

Much work has been directed to the investigation of the encephalitogenic reaction described in Vol. VI, p. 532. The nature of the agent has been investigated by Edward and its action on the central nervous system by Gaupp in his contribution to a combined paper on Hodgkin's disease by Uhlenhuth, Wurm, Liebegott and Gaupp. Edward produced evidence that the agent was not a virus: it was not deposited by high speed centrifugalization, using centrifuges which deposit the smallest viruses, the agent cannot be transmitted from one animal to another, it does not multiply in tissue cultures, or produce inclusion bodies in the affected brains.

The question of the identity of the encephalitogenic agent from the glands of Hodgkin's disease with that obtained from normal bone marrow has not been settled, this will probably be decided only when an antibody has been made from one and tested against the other.

Madding, in reporting 6 cases of Hodgkin's disease of the stomach, concludes that clinically it is impossible to distinguish this rare condition from ulcer and from carcinoma of the stomach, and that, although there are not any absolutely characteristic features radiologically, the presence of a diffuse lesion is suggestive. In 5 out of the 6 cases carcinoma was diagnosed before operation, and 3 of these patients were living 6 or more years after partial or complete resection of the stomach.

Differential diagnosis from histiocytic medullary reticulosis

Scott and Robb-Smith report 4 cases, and collected 6 previously published cases which constituted a clinical and pathological entity for which the term histiocytic medullary reticulosis was suggested. These cases had been regarded as a form of atypical Hodgkin's disease, but the two conditions were quite different and were not related in any way.

The clinical picture of histiocytic medullary reticulosis begins with asthenia, emaciation, profound intoxication, and high, sometimes relapsing, fever. The lymphatic glands were enlarged in 9 of the 10 cases, splenomegaly was present in all, the liver palpably enlarged in 8, and in the later stages jaundice occurred in 7. Anaemia was constant and more often normocytic than macrocytic, leucopenia was present in 7 cases, being so severe in 2 as to be associated with necrotic angina.

The course of the disease was rapid, from 6 to 32 weeks, the mean duration being 15 weeks. All the cases were in adults, and terminated fatally. Pathologically there was a systematized cellular proliferation throughout, and confined to, the lympho-reticular tissues with siderosis most intense in the hepatic parenchyma and Kupffer's cells. The cellular proliferation and active phagocytosis were predominant in the medulla of the lymphatic glands, the proliferation in the medulla was composed of reticulum cells, large lymphocytes, and large pro-histiocytes, 12 to 14 μ in diameter with nuclei averaging 9 μ in diameter. In the spleen infarcts were frequent, but the lymphatic nodules (Malpighian bodies) were not prominent. The bone marrow was commonly red, haemorrhagic, and with firmer scattered white nodules.

TREATMENT

Sensitized vaccine

Gordon reports (personal communication) on the effect in 2 cases (which occurred in Chile) in which lymphadenoma sensitized vaccine was administered. The strength of the vaccine was 1:100,000 and the elementary bodies had been flocculated with antiserum twice over. In the first patient, a man aged 22 years, with glandular enlargement for 6 years proved by biopsy to be Hodgkin's disease, subcutaneous injections, commencing with 0.1 cubic centimetre and increasing by 0.1 cubic centimetre, were given weekly up to 1.3 cubic centimetres. With the first injection loss of weight and an evening temperature up to 38.5° C were observed. After the fourth injection the temperature was normal, but the other symptoms persisted. After the seventh injection pain in the bones ceased, but perspiration and itching were noted. After the eleventh dose the leucocyte count was normal, but the neutrophilia remained high although the pathological changes in the cells had disappeared. The symptoms of mediastinal compression which had begun to diminish after a few previous injections disappeared after the twelfth injection. The thirteenth injection produced a temperature of 40° C which lasted for 3 days. Treatment was then stopped as the practitioner had not sufficient experience about its continuation. In the second patient, a man aged 28 years, with a 6-year history of Hodgkin's disease, some anaemia was present together with symptoms of mediastinal compression, diarrhoea, itching and perspiration, after the seventh injection all symptoms disappeared except the anaemia, for which he refused blood transfusion and from which he died.

Gordon recommends that the vaccine be given in small doses in order to avoid reactions, which are inadvisable, but he raises the question whether or not larger doses as mentioned in his Chilean reports should be used in cases at an early stage in the disease.

Baker, C., and Mann, W. N. (1939) *Guy's Hosp. Rep.*, 89, 83.

Edward, D. G. ff. (1938) *J. Path. Bact.*, 47, 481.

Madding, G. F. (1938) *Proc. Mayo Clin.*, 13, 618.

Scott, R. B., and Robb-Smith, A. H. T. (1939) *Lancet*, 2, 194.

Uhlenhuth, P., Wurm, K., Liebegott, G., and Gaupp, R., Jun. (1939) *Z. ges. exp. Med.*, 105, 205.

HYDATID DISEASE

PRIMARY CYSTS

Diagnosis of rupture

Casoni's test

- 692 Sergeant, Fourestier and Galliano while recognizing the value of Casoni's intradermal injection of hydatid fluid for the diagnosis, often difficult, of hydatid disease, draw attention to two limitations of practical importance: (1) Addition of an antiseptic to the hydatid fluid used for the test should be avoided. (2) The first time that the test is performed on a patient with hydatid fluid (without an antiseptic) it is valuable, but subsequent tests may give a fallacious positive result because the patient was sensitized by the fluid injected at the first test and therefore these tests should not be regarded as decisive.

MISCELLANEOUS CYSTS

Hydatid disease of mammary gland

- 700 Rinz has given the largest and most authentic statement on this rather rare type of hydatid disease and has collected records of 131 cases, including 2 in males. The author agrees that the parasite reaches the breast through the blood stream and that the more common occurrence in women is due to the greater development and physiological activity with consequent greater blood supply. The only pathological

type so far recorded is the unilocular cyst, inasmuch as the 2 cases classed in the literature as the alveolar form do not bear close scrutiny. The onset is insidious, the cyst often passing unnoticed for a long time until it reaches a large size or some complication ensues, or until it is made more obvious during pregnancy or breast feeding. The diagnosis is seldom made, because this type does not occur often and because of its confusion with other commoner cystic conditions. Careful study of the history and of the biological reactions, however, should make its diagnosis possible. The treatment is essentially surgical.

Cysts of the pancreas

A thesis by Ouvry is based on a study of 47 collected cases of hydatid disease in the pancreas, and contains an account of Deve's experimental work in which he obtained cysts of this organ in a massive infestation. Ouvry points out the rarity (0.2 per cent) of localization of the disease in this organ, and emphasizes the primary nature of the cysts and the fact that as a rule they are single and isolated, more often than not containing daughter cysts. As might be expected, the main clinical finding in cysts of the head is obstructive jaundice with varying degrees of pain, whereas in other parts of the organ the only finding is a rounded swelling which must be distinguished not only from pseudo-cysts and other pancreatic cysts but also from cysts of the left lobe of the liver, or of the kidney or the spleen. The diagnosis is therefore difficult, not often made pre-operatively although the position, biological tests or a trace of calcification in the adventitia might lead to a correct diagnosis. The treatment is surgical evacuation after preliminary formolage with or without drainage afterwards, the only risk being a persistent fistula. For this reason any attack on the fibrous adventitia is absolutely forbidden. There is a good bibliography.

TREATMENT

The use of aspiration methods during operations on hydatid disease

Finochietto deals in detail with his technique of evacuating hydatid cysts at operation by means of a large-bore cannula of special design combined with high negative pressure. He has found it of great value in achieving total removal of fluid, debris, daughter cysts, and even the whole of the mother cyst in a simple cyst, and so precluding any contamination of the operative field by hydatid elements. In spite of the objections which have been raised against the use of high negative pressure, which may cause eversion of the adventitious capsule and haemorrhage, and in spite of the slight risk of contamination by leakage alongside the tube and of the difficulties sometimes experienced because of multilocular cysts, Finochietto still finds his special cannula of great value.

Finochietto, E (1938) *Arch Internacionales de la Hidatidosis*, **14**, 145

Ouvry, A (1938) *Contribution a l'etude des kystes hydatiques du pancreas* Thèse de Paris, Paris

Rinz, V (1937) *Thesis*, Buenos Aires

Sergent, E., Fourestier, M., and Galliano, E. J (1939) *Bull Acad Med Paris*, **121**, 180

HYDROTHERAPY

EXTERNAL APPLICATION (BALNEOTHERAPY)

Baths

Immersion baths

Ten years' progress in hydrotherapy—In measles and scarlet fever the immunizing function of the skin can be stimulated by bathing. Mild neuroses also of doubtful aetiology generally clear up after a course of hydrotherapeutic treatment. Behrend refers to what is termed the 'bath reaction' (cure crisis) and states that this condition shows itself after the first 7 or 8 days of treatment in general fatigue and an increase of the original pain with restlessness. These reactions soon disappear after further treatment has been carried out. At the end of 3 weeks there may be a second type of reaction, this being characterized by slight elevation of blood pressure, increase of leucocytes and an increased blood sedimentation rate, sleeplessness and constipation are the outstanding symptoms (Behrend).

The therapeutic pool—Ray points out that the after-effects of war injuries in rheumatic subjects are liable to be complicated by a much protracted convalescence, with much more pain and muscular stiffness than would be expected in ordinary cases. By war injuries is meant not only gunshot wounds but also every kind of trauma, such as exposure to cold and damp and other adverse conditions physical and mental. He draws attention to the opinion of many observers that one of the essential causes of the rheumatic syndrome is an inefficient cutaneous circulation. Hence he pleads for the more extensive use of the therapeutic pool for war injuries, and believes that even better results may be expected from its use in the treatment of pain, stiffness and deformity occurring in younger and

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healthier patients Ray's inquiries showed that only a few institutions in this country have installed therapeutic pools, and quotes Lowman of America who states that they are extensively used there Basing his observations on well known principles of physics, Ray states that muscles sufficiently healthy to contract definitely but unable to move a joint out of water can often function in water This is because the body is supported at all points in water, and a good example is often seen in the stiffened and painful hip joints in cases of morbus coxae senilis patients who have to be wheeled or carried and lowered into the pool can at once walk in the water with apparent ease

Ray concludes 'It appears therefore that the therapeutic pool occupies a position midway between ordinary massage and electrotherapy, and occupational therapy It is only necessary to see a therapeutic pool in use and talk to the patients undergoing treatment to be convinced of its efficacy'

Galvanism applied in a full bath—This type of treatment is excellent in rheumatic conditions, especially when pain is the main symptom The water distributes the local stimulations over the whole of the skin Each treatment lasts for from 15 to 45 minutes A warning must be given with regard to the exacerbation of symptoms after from 2 to 4 treatments have been carried out Rest is essential after the bath for at least half an hour and may be required for one hour (Behrend)

Steam or hot air baths

The steam jet is now very much in use and by certain authorities is regarded as indispensable, physiologically the reaction is one of dilatation of the cutaneous capillaries and there is a considerable hyperaemia afterwards In sciatica and in acute bursitis of the shoulder pain is very much relieved (Behrend)

Behrend, H J (1944) *Arch phys Ther*, 25, 5

Ray, M B (1940) *Lancet*, 1, 683

HYPERCHLORHYDRIA

DEFINITION

Erratum

In Vol VII, p 2, second line from foot, for 'hydrogen concentration' read 'hydrogen ion concentration'

PHYSIOLOGY, PATHOLOGY AND PATHOGENY

Hollander surveys the various possible factors which may play a part in maintaining the normal level of gastric acidity by lowering the concentration from approximately 0.6 per cent, at which it is poured into the gastric cavity from the parietal cells, to the lower level normally found in test-meal examinations (1) The test meal dilutes the secretion, the authors, however, have devised a method of correcting for this (2) Saliva has a diluting and a neutralizing effect, which can be reduced by getting the patient to expectorate his saliva during the investigation (3) Regurgitation of duodenal contents appears to be a minor factor (4) Variations in the composition of the parietal secretion are probably slight (5) The possibility of re-absorption of hydrochloric acid by the gastric mucosa has not yet been adequately studied (6) There is strong evidence that the chief factor in lowering the gastric acidity is the production by the mucosa of one or more non-acid buffer-containing fluids, which also act by diluting the acid The part played by pepsin in this direction is probably negligible, there is much more evidence for the existence of a specific non-acid diluting secretion which exerts an influence in the regulation of acidity, the arguments for and against the importance of mucus in this respect are at present contradictory

TREATMENT

Drugs

Necheles, Neuwelt, Steiner and Motel studied the toxicity and pharmacological action of the antispasmodic drug trasentin (diphenylacetyldiethylaminoethanoylester hydrochloride) The drug was found to be 10 times more toxic to the dog than to the rat, 100 milligrams per kilogram of body weight being the minimum lethal dose for the dog In the human, single oral doses of 150 milligrams and daily oral doses of 450 milligrams continued for several weeks did not have any harmful effects In its action this substance combined the properties of atropine and papaverine in that it abolished spasmodic contractions of smooth muscle produced either by direct stimulation or by indirect stimulation through the parasympathetic nerves

Einhorn emphasizes the absence of toxic effects and of side-effects, such as dryness of the mouth, dilatation of the pupils and circulatory disturbances

Bennett and Gill investigated on a small series of hospital patients the claims made for colloidal aluminium hydroxide in the treatment of peptic ulcer (gastric, duodenal and anastomotic) It has been claimed that aluminium hydroxide gel is preferable to alkalis for this purpose because, being amphoteric, it can neutralize hydrochloric acid without becoming basic, and that, in fact, it cannot produce an alkaline reaction In 30 patients with peptic ulcer the gel was effective and did not produce alkalosis

Bennett, T I, and Gill, A M (1939) *Lancet*, 1, 500Einhorn, M (1938) *Amer J digest Dig*, 5, 121Hollander, F (1938) *Amer J digest Dis*, 5, 364Necheles, H, Neuwelt, F, Steiner, N, and Motel, W G (1939)
Amer J digest Dis, 6, 39

HYPOGLYCAEMIA AND HYPERINSULINISM

Corrigenda

In Vol VII, p 43, l 17, in the paragraph, *Spontaneous hypoglycaemia*, for 'has been reported' read 'is to be expected'

On p 44 in the paragraph, *Changes in central nervous system*, after the first sentence read the following in place of the remainder of the paragraph 'The histology is like that of anoxia or oxachrestia, there is degeneration and necrosis in scattered areas of the cerebral cortex with disappearance of nerve cells. There may be selective involvement of the outer or inner laminae, and of parts of the hippocampus major. The corpus striatum and to a lesser extent the cerebellum are also affected.'

On p 46 for the paragraph, *Time of action of insulins*, substitute the following 'Ordinary insulin exerts its main effect 18 hours after injection, protamine insulin 6 hours and protamine zinc insulin 24 hours or longer, the larger the dose the more prolonged the action (Bennett and others, Lawrence and Archer).'

AETIOLOGY

The following non-pancreatic cases have been reported (1) With Simmonds's syndrome, one case (Mogensen), (2) pituitary disease, 4 cases, including one case of hypopituitarism (Chaves), one of Frolich's syndrome (Hart), one with an infarct of the anterior lobe of the pituitary body (Kotte and Vonderahe) and a case of hypoglycaemia after encephalitis, reported by Meakins who thought there was probably a hypothalamic lesion.

Hart and Lisa report the rate of occurrence of hypoglycaemia in routine fasting blood sugar estimations in 21,000 patients. The blood sugar was below 79 milligrams per 100 cubic centimetres in 2,371 cases, and below 70 milligrams per 100 cubic centimetres in 751 cases.

Experiments have been made on rabbits, an intraperitoneal inoculation of a synthetic styryl-quinoline being made, or an intravenous inoculation of alloxan. The result was that almost all the island tissue of the pancreas became necrosed. As the lesion developed there was a rise in blood sugar followed by an intense hypoglycaemia (Dunn, Sheehan and McLetchie). This condition causes a fatal end in from 12 to 48 hours. The suggestion that the lesion may be produced by overstimulation of the islands, with overproduction of insulin and later death of cells from overstrain, has been reported by Lawrence, who questions the interpretation of the signs and suggests that the changes in blood sugar may be due to toxic effects on the liver.

MORBID ANATOMY

Changes in the central nervous system

Hypoglycaemia and the brain

In a review of 6 fatal cases of hypoglycaemia Lawrence, Meyer and Nevin state that the length and the seriousness of the hypoglycaemia were not known accurately. As a rule the damage to the nerves seemed to be enough to cause death, directly or indirectly, but it is probable that in two cases cardiac failure was the basis of the breakdown.

CLINICAL PICTURE AND COURSE

Chronic spontaneous hypoglycaemia

Insulin hypersensitivity

Allen suggests that patients become sensitive to insulin after repeated doses, and instances non-diabetics who thrive and put on weight on from 50 to 75 units a day, but in whom there develop symptoms of intoxication after weeks or months. This may, in part, explain the intermittency of symptoms in patients with islet-cell tumours.

Insulin shock therapy

Billig, writing on insulin shock therapy, states that the dose necessary to produce shock varies from patient to patient, and even in the same patient, the lowest necessary for deep coma being 18 units, and the highest being 400 units. He divides the stages into sub-shock (somnia, euphoria, perspiration, hypotonus), medium coma (clouding of consciousness, functions slow, sometimes motor excitability), deep coma (vital centres depressed).

Complications—There may be convulsions which are not dangerous, sudden respiratory or motor failure, and lastly and most dangerous, protracted coma, which lasts for hours or even days after the blood sugar is restored to the normal.

Diet

Allen advocates a moderate amount of carbohydrate in the diet and he observed that excessive doses of glucose stimulate the islet cells to secrete, and that small

frequent feeds of a slowly absorbed carbohydrate are more effective in preventing hypoglycaemia

Criminal behaviour

Wilder states that there is a distinct relation between subnormal blood sugar and criminal behaviour. He gives a long list of crimes and offences proved or suspected in the hypoglycaemia state, including disorderly conduct, assault and cruelty. He further states that problem children are often hypoglycaemic.

Infants of diabetic mothers

Miller and Ross write on the relation of hypoglycaemia to the symptoms observed in infants of diabetic mothers, and report 6 cases. Four of the children were free from symptoms, the lowest blood sugar being less than 10 milligrams per 100 cubic centimetres. In the 2 cases with symptoms these were not improved by intravenous glucose and the symptoms were explained by organic disease, one child having an enlarged liver and the other erythroblastosis foetalis and cerebral injury.

The blood sugar in the first 48 hours of life is compared in normal full-term and premature infants with those born of diabetic mothers.

		NORMAL FULL-TERM	PREMATURE	BORN OF DIABETIC MOTHERS
Number of infants	- - -	17	20	6
Number of blood sugar estimations	-	28	40	17
Blood sugar average in milligrams per 100 cubic centimetres	- - -	49.9	31.8	29.7

The blood sugar in infants born of diabetic mothers was lower than that of full-term children, but approximated to that of premature infants, and the writers conclude that even very low blood sugars in the first 48 hours of life do not produce symptoms.

Potter, Seckel and Stryker state that hypertrophy and hyperplasia of the islands of Langerhans in the foetus or the new-born infant may be found in association with maternal diabetes or when the mother is non-diabetic. It is occasionally found in infants suffering from erythroblastosis.

Coeliac disease

May and McCreary give evidence to show that the low blood sugar curve which is almost constant in coeliac disease and in other conditions such as sprue, cretinism, disease of the pancreas, and malnutrition, is due to delay and irregularity in gastrointestinal mobility which cause deficient absorption.

Pancreatotomy

David considers the indications and results of pancreatotomy in hypoglycaemia. He reviews the literature and observes that when partial resection included an islet-cell tumour the results were highly successful.

Experimental work

Keller shows that hypothalamic lesions in dogs produce increased insulin sensitivity and hypoglycaemia. Gellhorn, Kiely and Hamilton studied hypoglycaemic and anoxic convulsions in rabbits, and show that anoxia prevents insulin convulsions.

Yesnick and Gellhorn studied the effect of increased intracranial pressure during anoxia and hypoglycaemia. They found that inhaled oxygen (7-8 per cent) has the same effect as hypoglycaemia on the blood pressure response to increased intracranial pressure; their experiments suggest that an adrenergic hormone is released in hypoglycaemia.

Marble, Fernald and Smith seek proof of a diabetogenic hormone by noting the effect of human diabetic plasma on the blood sugar curve after insulin in rabbits. The plasma of only 2 patients out of 30 had any effect and that was inconstant.

Allen, F. M. (1941) *J. clin. Endocrinol.*, **1**, 595

Billig, O. (1941) *Sth. Med. Surg.*, **103**, 646

Chaves, N. (1940) *Neurobiologia*, **3**, 147

David, V. C. (1940) *Surgery*, **8**, 212

Dunn, J. S., Sheehan, H. L., and McLetchie, N. G. B. (1943) *Lancet*, **1**, 484

Gellhorn, E., Kiely, W. F., and Hamilton, S. L. (1940) *Amer. J. Physiol.*, **130**, 256

Hart, J. F. (1940) *Endocrinology*, **27**, 759

— and Lisa, J. R. (1940) *Endocrinology*, **27**, 19

Keller, A. D. (1939) *Proc. Soc. exp. Biol., N.Y.*, **42**, 837

Kotte, J. H., and Vonderahe, A. R. (1940) *J. Amer. med. Ass.*, **114**, 950

Lawrence, R. D. (1943) *Lancet*, **1**, 600

— Meyer, A., and Nevin, S. (1942) *Quart. J. Med. N.S.*, **11**,

IMMUNITY AND IMMUNIZATION

- Marble, A., Fernald, Alison T., and Smith, Rachel M (1940) *Endocrinology*, **26**, 735
May, C D., and McCreary, J F (1940) *J Pediat*, **17**, 143
Meakins, J C (1940) *Ann intern Med*, **13**, 1830
Miller, H C., and Ross, R A (1940) *J Pediat*, **16**, 473
Mogenssen, E (1940) *Endocrinology*, **27**, 194
Potter, Edith L., Seckel, H P G., and Stryker, W A (1941) *Arch Path*, **31**, 467
Wilder, J (1940) *J crim Psychopath*, **1**, 219
Yesinick, L., and Gellhorn, E (1939) *Amer J Physiol*, **128**, 185

IMMUNITY AND IMMUNIZATION

ACTIVE IMMUNITY

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In a review of his observations recorded during a period of 12 years, Ramon discusses the effect on active immunization of various procedures which tend to decrease the toxic effects of immunizing injections, and increase the production of antibodies. The methods studied include the addition to the injected toxin or toxoid of substances such as tapioca, lanolin, and liquid paraffin, and the administration of repeated minute doses of toxin into the same area of subcutaneous tissue. The method of adding lanolin to the inoculum has also been applied to living bacteria such as *Corynebacterium diphtheriae*, *Bacillus anthracis*, and staphylococcus.

Analogous observations were made by Glennon on the use of alum precipitated toxoid, and by Schmidt on toxoid precipitated by aluminium hydrate. According to Ramon, the lowering of toxicity and increase in immunizing potency induced by such procedures are due not to a direct action of the added material on the antigen concerned but to an effect exerted on the animal's tissues. This effect depends upon an increase in the local inflammatory reaction with an associated delay in the rate of absorption. Of these two factors, the inflammatory reaction is probably the more important, since it has been shown that repeated subcutaneous injections of minute amounts of toxin produce a lessened toxic, but an increased immunizing, effect when the injections are given into the same site instead of into many different sites.

Another approach to the same problem, that of increasing the immunizing potency while diminishing the toxicity of antigens, especially bacterial antigens, may be found in attempts to isolate from whole bacteria the different chemical fractions upon which their antigenicity depends. Most bacteria contain a multiplicity of such fractions, many of which are of little or no importance in the production of protective antibodies against the complete organism. In the case of some bacterial species, for example *Streptococcus pneumoniae*, it has been possible to isolate in a fairly pure state those fractions upon which the production of protective antibodies in the immunized animal depends. Ekwurzel and his fellow-workers record field trials in the production of active immunity against pneumonia by single injections of purified pneumococcal polysaccharide. Topley and his colleagues isolated from *Bacterium typhosum* a chemically pure and stable antigen having the immunizing properties of the whole bacterial cells. The result of field trials in the use of such a fraction for the production of typhoid immunity will be awaited with interest.

PRACTICAL APPLICATIONS OF IMMUNITY

Diphtheria

Schick test

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Although the Schick test is undoubtedly of great value, it shares with other biological tests the defect of individual variation. It is becoming increasingly realized that there is not an exact level of antitoxin, but a Schick 'zone of immunity', which separates Schick positive from Schick negative individuals (Jensen, Parish and Wright¹). In general, it appears that 50 per cent of persons with from $\frac{1}{300}$ to $\frac{1}{100}$ of a unit of antitoxin per cubic centimetre in their blood are Schick negative, fewer persons with $\frac{1}{300}$ and only exceptional individuals with $\frac{1}{1000}$ are negative. Similarly the zone extends in the other direction, but it is very rare to find a positive reactor with as much as $\frac{1}{30}$ unit.

Diphtheria in Schick negative reactors—A number of cases of diphtheria, almost invariably mild, have been reported from time to time in Schick negative reactors. The level of antitoxin corresponding to the negative reaction has been inadequate to ensure protection either because the infecting dose has been large or the strain of *C. diphtheriae* has been of unusually high virulence. For this reason many clinicians consider it advisable to inject one dose of diphtheria prophylactic into all 'natural' Schick negative persons at the time of the Schick reading.

'Relapse' from Schick negative to Schick positive—The titre of circulating antitoxin tends to wane in subjects who have few opportunities of contact with cases or carriers of toxigenic *C. diphtheriae*, for example in country districts and in certain institutions. The cells of the body, however, retain potential immunity throughout life, that is the power of rapid response to specific stimuli so that adequate antitoxin is produced when required. Diphtheria in individuals who have formerly been Schick

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negative is relatively infrequent, and is usually mild. A number of cases are on record in which rapid recovery has taken place without treatment with antitoxic serum.

Re-inoculation of prophylactic—To obtain a durable immunity to diphtheria, it may be necessary to give periodic re-injections of T A F or A P T (Parish and Wright²). In some hospitals it is the practice to give members of the nursing staff one or more injections of T A F every year. Children who have received 2 doses of A P T in infancy may be given a third dose at the time of entry into school, and possibly a fourth dose at the age of 9 years. If children were re-inoculated as a routine in a community, the use of the Schick test might safely be curtailed.

Tetanus and gas gangrene

Ramon and his colleagues have described a method for the rapid induction of antitoxin immunity against tetanus or diphtheria. This consists in the simultaneous injection of antitoxin and toxoid, followed at suitable intervals by 2 further injections of toxoid. Experiments on rabbits indicate that the injection of a dose of antitoxin at the same time as the initial dose of toxoid exerts no inhibitory effect on the production of antitoxin by the animal's tissues in response to the stimulus provided by the toxoid.

Streptococcal infections

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Artificial immunization in the treatment of streptococcal infections has recently been partially eclipsed by chemotherapy. The mode of action of compounds of the sulphonamide group in combating infection remains obscure, but probably differs from that of immune bodies.

Enteric fevers

Vi-antigen

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Serum prepared by the method recommended by Felix, and having a high content of Vi in addition to H and O antibodies, has received therapeutic trial in the treatment of typhoid fever in 5 reported investigations (Felix, Robertson and Yu, McSweeney, Cookson and Facey, Pijper and Crocker). In all 5 instances the serum has been found of value, but, apart from those cases reported by Felix, adequate controls have been lacking.

Cookson, H., and Facey, R. V. (1937) *Brit med J*, **1**, 1009

Ekwurzel, G. M., Simmons, J. S., Dublin, L. I., and Felton, L. D. (1938) *Publ Hlth Rep, Wash*, **53**, 1877

Felix, A. (1935) *Lancet*, **1**, 799

Glenny, A. T., and Llewellyn-Jones, M. (1938) *J Path Bact*, **47**, 405

Jensen, C. (1931) *C R Soc Biol Paris*, **108**, 539, 543, 552, 577, 579

McSweeney, C. J. (1937) *Brit med J*, **2**, 1118

Parish, H. J., and Wright, Joyce (1935)¹ *Lancet*, **1**, 600

— (1938)² *ibid*, **1**, 882

Pijper, A., and Crocker, C. G. (1939) *S Afr med J*, **13**, 255

Ramon, G. (1938) *Rev d'Immunol, Paris*, **4**, 5

— Boicin, A., Richou, R., Djourichitch, M., and Maccolini, R. (1938) *Rev d'Immunol, Paris*, **4**, 24

Robertson, R. C., and Yu, H. (1936) *Brit med J*, **2**, 1138

Topley, W. W. C., Raistrick, H., Wilson, J., Stacey, M., Challinor, S. W., and Clark, R. O. J. (1937) *Lancet*, **1**, 252

IMPETIGO

ACUTE IMPETIGO

Aetiology

734

Impetigo is apparently on the increase. There is considerable difficulty in managing it and the use of sulphonamides for treatment has resulted in much alteration in the basic therapeutic methods.

Treatment

It is essential to note that in the main the treatment of impetigo is a nursing problem. When sulphonamides are used the time required in order to obtain a cure is from 3 to 8 days. Sulphanilamide, sulphathiazole and sulphadiazine have all been tested and have acted successfully in streptococcal cases. If the sulphonamide is in a concentration higher than 5 per cent, local reactions must be expected and on account of the latter also the treatment should be of a duration not longer than 6 or 7 days. The giving of sulphonamides by the mouth is still in its early stages, and as yet there is not any settled plan of action with regard to it. So far as the vehicle in which sulphonamides are applied to the skin is concerned, lanette wax SX type (cetyl alcohol) makes it possible for the creams and pastes to be made up without lanolin or paraffin. Sulphonamides are most active in such bases, and serous discharges are most easily absorbed. The use of cetyl-trimethyl-ammonium bromide (C T A B) as a method of cleansing is increasing.

Treatment

The sulphonamide group of drugs can be given to patients with confluent impetigo of the scalp and face of the type shown in Vol VII, p 95, this treatment is particularly suitable for adults but may also be used for children. The dose for adults is one 0.5 gramme tablet 3 times daily for 10 days. Children and adults who have not responded well to prolonged local treatment have definitely improved with a sulphonamide compound but the drug must be given with great caution.

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INDUSTRIAL ACCIDENTS

Corrigendum

In Vol VII, p 122, line 22 'Factory and Workshop Act, 1901' should be altered to 'Factories Act, 1937'.

Addendum

On p 122, paragraph 5 the figures for 1938 are as follows. The chief Inspector of Factories reported (1938) that as a result of 308,061 visits paid to 549,972 factories and workshops in the year 1937, notices of contravention of regulations were served in 240,774 cases, 2,347 prosecutions were instituted against 853 firms, 336 of these charges were in respect of accidents entailing injury or death of workers.

COMPENSATION FOR DISABILITY DUE TO INDUSTRIAL ACCIDENTS AND DISEASES

Lump sum' settlements

It is the usual practice in industry to engage workmen by the week, and to pay weekly wages, following this convention, the industrial worker is accustomed to a weekly budget, so that payment of compensation is conveniently made in the same manner. In some cases, these payments may be commuted for a single payment, or 'lump sum', intended to redeem future liability. This is, for instance, provided for by Section 13 of the Workmen's Compensation Act, 1925, under which an employer is entitled to redeem his future liability in cases in which weekly payments have been made for not less than 6 months, the amount laid down as appropriate is such as would purchase an annuity from the National Debt Commissioners equal to 75 per cent of the weekly payments. This sum may be applied by the Court to the benefit of the injured workman.

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It is, however, a common practice to negotiate a cash settlement once and for all of claims under the Acts even when disability has not lasted for 6 months, and for amounts which may be considerably less than the value of such an annuity. When liability under the Acts is disputed, the employer or his insurance company may propose a 'composition agreement', that is a settlement 'without prejudice', he may say, in effect, 'If I am liable to pay compensation at all, I should have to pay £100, it would cost me £50 to take the case to Court to test the question of liability, very well, I will pay you £50 to get rid of any liability in respect of this accident'.

Much hard bargaining takes place over such negotiations, in which the workman is often badly handicapped by lack of expert advice. An employer is not relieved of his liability by such an agreement unless it is registered in the County Court, but workmen do not always know this, and Courts are not always particularly careful to protect the interests of the workman. Wilson and Levy dealt exhaustively with the disadvantages of 'lump sum' payments, and these are severely criticized in the report of the International Labour Office on the Evaluation of Permanent Incapacity for Work in Social Insurance (1937).

SUMMARY AND CONCLUSIONS

Wilson and Levy have published a careful study, with abundant references to authorities, dealing with many of the problems of industrial injuries, including an historical review of the workmen's compensation laws in Great Britain, and making valuable suggestions for improving these.

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In 1936 an Interdepartmental Committee was appointed to report on the 'Rehabilitation of Persons Injured by Accidents', and this Committee issued an Interim Report in 1937 dealing with the treatment of fractures. Many cases of this type arise in industry, and form a substantial proportion of the more serious injuries.

Ministry of Health (1937), *Interim Report of the Interdepartmental Committee on the Rehabilitation of Persons injured by Accidents*, London.

Wilson, A., and Levy, H. (1939) *Workmen's Compensation*, Vol 1, *Social and Political Development*. London.

**INFANT FEEDING THE FEEDING OF NORMAL INFANTS
AND CHILDREN**

BREAST FEEDING

Quantity of milk secreted

- 750 Secretion of breast milk can be stimulated by the lactogenic hormone of the anterior pituitary, it can be inhibited by the follicular hormone, any preparation of which, such as oestrone, can be used with success when for any reason inhibition of lactation is necessary or desirable

Relation of maternal diet to lactation

Drugs of the sulphanilamide group administered to the mother during lactation are secreted in breast milk, but not in sufficient quantity to be of any significance or to affect the infant

General management

Waller, whose work *Clinical Studies in Lactation* is to be recommended, made important communications to the *Lancet* in 1943. He is particularly emphatic that in the first 4 weeks failure in breast feeding is due often to mechanical causes and he discusses the physiology of a typical breast feed

**WET-NURSING AND FEEDING WITH ARTIFICIAL FOODS
UP TO AGE OF NINE MONTHS**

Soya bean flour

- 751 In many parts of the world artificial feeding is a serious problem owing to the absence or prohibitive cost of substitutes for breast milk. Mackay has experimented with a mixture of equal parts of dried milk and soya bean flour (soyolk), this proved very satisfactory and the cost was little over half that of dried milk. This proprietary preparation, called yolac, was mixed with water in the proportion of 1 in 8. The calorie value of this strength of mixture is about the same as that of cows' milk. The iron content of soya beans is much higher than that of liquid milk, and the iron content of yolac is approximately 5 times that of dried full-cream milk, this is important in view of the frequent occurrence of anaemia in young children fed on a milk diet. The vitamin A content is said to be similar to that of cows' milk, the content of vitamin B complex appears to be satisfactory, that of vitamin D is inadequate for tropical countries, and vitamin C can be supplied by fresh fruit or vegetable juices. Since the outbreak of war in 1939 these juices have been difficult to procure, and to replace the vitamin C contained in them, certain preparations such as celn tablets have been put on the market, they are most useful in this connexion. The Ministry of Health distributes fruit juice and cod-liver oil compound free to children up to the age of 5 years if the family income is below a certain limit.

Rose hip syrup or jelly provides a suitable and inexpensive form of vitamin C for administration, the dose for children is from 4 to 8 milligrams of the jelly or from 1 to 2 fluid drachms of the syrup, black-currant syrup is also available as a substitute for oranges for children. Rose hips contain from 0.4 to 1 per cent of ascorbic acid, and are four times richer than black currants and twenty times richer than oranges in vitamin C.

Mackay, H. M. M. (1940) *Arch. Dis. Childh.*, **15**, 1.

Waller, H. K. (1939) *Clinical Studies in Lactation* London.

— (1943) *Lancet*, **1**, 69.

INFLUENZA

DEFINITION

- 754 The amount of work which has been done on atypical pneumonia is likely to assist materially in clearing up many of the doubts which exist with regard to the clear definition of the term, influenza.

TREATMENT

Preventive

If a mask is worn during attendance on influenza patients it should protect the eyes, as infection can enter by this route. It is difficult to isolate infective persons but masks can be worn by nurses, they are not a practical proposition so far as the community is concerned. Neither gargling, nor douches, nor sprays, nor aerosol mist is better than fresh air.

With regard to immunization there are so many variations (virus A, virus B and the grade known as influenza Y) and substrains that vaccination cannot succeed in universal immunization. Any protection that might be afforded is likely to last for a very short time only and it would have to be renewed at the beginning of each winter. The serum therapy of influenza is still in the experimental stage and there is not much hope of obtaining positive results.

There is no specific treatment for influenza, and it is not yet possible to immunize persons against the disease. Experiments are being done with immunization in which known strains of influenza virus are used, but it is impossible to say what particular grade of influenza virus will be the predominant factor in any future pandemic.

INFANT FEEDING—INTELLIGENCE TESTS

Vol. VII
KEY NUMBERS
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Quarantine methods are not successful for more than a few months, except in very special cases. Every possible endeavour should be made however to keep the populations dispersed and to avoid crowding or intermingling.

INTELLIGENCE TESTS

TYPES OF INTELLIGENCE TEST

Individual verbal tests (the Binet Scale)

A Committee set up in 1938, by the National Institute of Industrial Psychology, to prepare an English standardization of the Terman-Merrill version of the Binet-Simon intelligence scale has almost completed its work. The publication of its results has been delayed by the present war.

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Group non-verbal tests

A non-verbal 'perceptual' test of intelligence, suitable for measuring intelligence in all subjects with a mental age above 3 years, has been prepared by Penrose and Raven, of the Research Department, Royal Eastern Counties' Institution, Colchester. These progressive matrices consist of 5 sets, each of 12 tests. A test is composed of a page of diagrams. The chief one is a rectangular figure covered by a geometrical pattern except in one area which is left blank. Below are 6 or 8 pieces the same shape and size as the blank area on the main diagram and covered with various patterns, the subject is asked to select the one which, when fitted into the blank area, would complete the pattern. A table of norms for subjects between the ages of 6 and 14 years is provided. The Penrose-Raven Progressive Matrices Test has taken its place among the widely used tests of intelligence. The publishers, H. K. Lewis & Co., Gower Street, London, W.C.1, have issued a table of norms which includes figures for adult males. The psychiatrists of the Royal Army Medical Corps make extensive use of the test and special Army directions for its administration have been printed. One of its merits is that it does not penalize the adult who is unaccustomed to reading, another that adults do not appear to feel insulted by it. Although the test is extremely valuable in discriminating between men of below-average intelligence, it is not particularly successful in separating those of high intelligence.

The American Army, developing the procedure it worked out during the war of 1914-18, has produced a new group non-verbal test which is clearly superior to the old Army Beta Test. The new non-verbal test—and, indeed, the new American Army verbal test too—makes extensive use of a 'counting cubes' type of problem in which the number of cubes in a pile has to be assessed, some of them are visible and some are invisible.

PRINCIPAL USES OF INTELLIGENCE TESTS

Experience with the Forces has shown once again the value of group paper-and-pencil intelligence tests. They are being used in all the Forces in Great Britain in the allocation of men to war-time employment. The Royal Navy has adopted, for use in the testing of men of apparently low grade intelligence, a modification of the Kohs Blocks Test, which is of the performance type, and a revision of the Wechsler Bellevue Intelligence Scale, which is an adult test of the Binet variety.

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In industry

Although it is unusual for a person to do himself more than justice in an intelligence test, it is by no means rare for an able individual to appear to be of mediocre intellect, or for a mediocre one to appear dull. Much depends upon the suitability of the test employed, upon the satisfactoriness of the conditions under which it is given, upon the physical and mental state of the person to whom it is given, and upon the skill of the giver. Even a highly skilled tester may be poorly qualified to pass an opinion on the significance of the results obtained.

An intelligence test is intended to provide an estimate of a person's intellectual capacity, rather than of his intellectual achievement. It is therefore necessary that, while he is being tested, nothing should interfere with his chances of displaying his powers to the full. An individual whose attention flags can often be dealt with appropriately by a tester of average skill, if he is being tested alone. If he is a member of a group, greater skill is required, because others may be distracted by the special attention he must receive.

But the difficulties attendant on the proper interpretation of an intelligence test score are even greater than those arising in the administration of the test. Here the psychologist finds even more justification for his inclination to regard the use of intelligence tests as a specialized task. He must proceed carefully towards a conclusion that a person, A, not only seems dull but is dull. He must proceed even more carefully towards a conclusion that A, a dullard, is certainly not fitted for occupation X, possibly not fitted for occupation Y, but perhaps adequately equipped intellectually for occupation Z. In fact, an intelligence test result can have little significance for anyone who does not have any relevant background against which to study it.

These considerations all lead to the conclusion that intelligence test results are not

CUMULATIVE SUPPLEMENT 1945

to be depended upon unless they have been obtained by a skilled tester, and to the further conclusion that their interpretation should be left in the hands of a skilled interpreter. Fortunately the supply of trained persons is likely to be considerably greater after the war than it has been previously, and in Great Britain, if not in the Dominions and Colonies, there are likely to be relatively few medical men who will not be within range of a hospital, clinic, school, teachers' training college or university psychological department able to offer facilities for the intelligence testing of children and young adults, and for the interpretation of test results. It is therefore probable that many doctors willing to attach importance to intelligence test results will, if they are not themselves skilled in the use of such tests, be able in future to call on the services of people with appropriate training and experience.

Penrose, L. S., and Raven, J. C. (1936) *Brit J med Psychol*, 16, 97

INTESTINAL OBSTRUCTION

ACUTE INTESTINAL OBSTRUCTION

General treatment

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Wangensteen, Rea, Smith and Schwyzer report the results of treatment of all cases of acute mechanical intestinal obstruction of the small intestine seen at the University Hospital, Minneapolis, between June 1931 and June 1938, there were 156 patients and 190 cases, some being recurrences. There were 28 deaths in the series. In 66.3 per cent of all cases and 61.5 per cent of all patients (126 cases and 96 patients) duodenal suction was the primary treatment, among these there were 15 deaths, giving a patient mortality of 15.6 per cent and a case mortality of 11.9 per cent. Of 83 of these patients suction alone accomplished a satisfactory decompression in 64, there were 5 deaths in this series, giving a patient mortality of 7.8 per cent and a case mortality of 6 per cent. The authors confirmed the importance of this method in suitable cases, but emphasized the importance of differentiating (1) simple and strangulating types of obstruction, and (2) acute obstruction in the large and small bowel.

Miller-Abbott tube

This is used for the treatment of intestinal obstruction. It should never be used if the blood supply may possibly be interfered with or when there is constant rather than intermittent pain. The tube is always contra-indicated in obstruction of the large bowel. It can be used in all cases of ileus. The Miller-Abbott tube is about 10 feet long and near its distal end is attached a balloon with means for inflation and deflation. Suction drainage is instituted when the tube tip enters the stomach, and when the distal end enters the duodenum like any other suction tube, the balloon is inflated. The peristaltic action now propels the balloon onwards, dragging the tube after it. Continuous suction ahead of the balloon is essential, as obviously it cannot be acted upon by peristalsis until the intestinal wall contracts on its surface. By means of this device the tube can be passed to the point of a mechanical obstruction or through the small intestine in a case of adynamic ileus.

Saline solutions

Jones and Morgan state that if a patient is given his normal requirement of 3,600 cubic centimetres of fluid in a day in the form of normal saline he will receive 32 grammes of salt, which is at least 6 times too much. Saline plus 5 per cent glucose is hypertonic in addition. Such fluids are therefore reserved for fluid replacement in emergency only. When continuous replacement is necessary they use one pint of normal saline to 4 of tap water per rectum, or one pint of saline to 4 or 5 per cent glucose intravenously.

Prevention of peritonitis

Hudson, Smith and Selbie point out that the mortality of intestinal obstruction is 6.7 per cent if simple release can be performed, but 77.4 per cent if resection is necessary. This mortality is to some extent due to peritonitis in the latter cases. Experiments show that peritonitis can be prevented by intraperitoneal giving of sulphanilamide. They have used from 10 to 15 grammes suspended in saline intraperitoneally in 2 cases of resection, both patients recovered.

PARALYTIC ILEUS

Decompression in ileus

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Decompression is also of immense value in post-operative distension or ileus, and this condition has lost many of its horrors in consequence. Dodd, writing on the passive treatment of ileus, is strongly opposed to the use of drugs for the purpose of stimulating the intestine, and relies upon decompression, fluids by every route, and morphine one-sixth of a grain with leptazol 1 cubic centimetre 4-hourly. Enemas are not allowed and the only active step is the passage of a flatus tube for 15 minutes twice a day. The treatment is continued until the pulse returns to 72, and nothing but water and fruit juices pass the lips. A chart of fluid intake and output is essential. Holt supports this view and finds that intestinal decompression has entirely supplanted enterostomy, for it has all the advantages and none of the disadvantages.

INTESTINAL OBSTRUCTION—JAUNDICE

These and other observations have led to the diminished use of drugs to stimulate the bowel, which at best were rather uncertain in their action. Prostigmin, in doses of 1–2 cubic centimetres, repeated in 4 hours if necessary, is of value in relieving simple gas pains and retention of urine after laparotomy, and is claimed to be of use in ileus and in acute dilatation of the stomach. In these latter conditions, however, decompression from above is essential, and is more likely to overcome the condition.

- Dodd, H. (1940) *Lancet*, 2, 98
Holt, R. L. (1939) *Lancet*, 2, 61
Hudson, R. V., Smith, R., and Selbie, F. R. (1941) *Lancet*, 1, 438
Jones, F. A., and Morgan, C. N. (1939) *Lancet*, 2, 611
Wangensteen, O. H., Rea, C. E., Smith, B. A., Jun., and Schwyzer, H. C. (1939) *Surg. Gynec. Obstet.*, 68, 851

INTESTINES, TUBERCULOSIS ULCERATIVE ENTEROCOLITIS

Treatment

Special dieting

A high calorie diet of approximately 3,200 calories has been recommended, the carbohydrate element predominates and bland foods with low residue are chosen. As a rule there are 5 meals a day. Peck and Jones state that ascorbic acid does not have any substantial effect, they treated 14 patients by saturation with ascorbic acid for 9 months and 8 patients were allowed to remain much below saturation point. It was found that the symptoms were controlled in both groups by diet only.

- Peck, W. M., and Jones, Julia M. (1943) *Amer. Rev. Tuberc.*, 47, 598

JAUNDICE

CLASSIFICATION OF JAUNDICE

Manson-Bahr states that in the Tropics jaundice may occur (1) in malaria, (2) in Oroya fever, (3) in kala-azar, (4) in relapsing fever, (5) in Weil's disease, (6) in yellow fever, (7) in amoebiasis, (8) in non-alcoholic cirrhosis of the liver and in various other diseases.

TREATMENT OF JAUNDICE

Of haemorrhage

The most important advance in the treatment of haemorrhage in jaundice has been the substitution and use of certain naphthoquinone substances in place of biological concentrates of vitamin K. This advance followed work which suggested that the active principle contained a quinoid group (McKee, Binkley, Thayer, MacCorquodale and Doisy), and finally the compound 2-methyl-3-phytyl-1,4-naphthoquinone was isolated (Binkley, Cheney, Holcomb, McKee, Thayer, MacCorquodale and Doisy, Almquist and Klose, Fieser, Campbell, Fry and Gates). A number of compounds containing a quinoid group have been tested therapeutically and several of them have proved to be more active than the older vitamin K concentrates. These quinoid compounds of known structure have obvious advantages in control of dosage and greater scope in methods of administration, and some of the undesirable side-effects—nausea, vomiting, diarrhoea—occasionally encountered when vitamin K concentrates and bile salts were given by mouth, appear to have been eliminated. Brinkhous has reviewed the quinoid compounds which have been tested therapeutically but only 3 with striking vitamin K activity are discussed here: kapilon (2-methyl-1,4-naphthoquinone) (Ansbacher and Fernholz, Macfie, Bacharach and Chance, Stein), hykinone (2-methyl-1,4-naphthohydroquinone-3-sodium sulphate) (Kark and Souter), and synkavit, the tetra sodium salt of 2-methyl-1,4-naphthohydroquinone-diphosphoric acid (Reid). Kapilon, a crystalline powder, sparingly soluble in water, may be given by mouth in tablet form in 10-milligram doses or by intramuscular injection of 5 milligrams in arachis oil. Hykinone and synkavit are more soluble in water and thus are suitable for intravenous injection. Hykinone is available in 1–3 cubic centimetre ampoules and has been given effectively intramuscularly and intravenously.

Synkavit, readily soluble in water, is supplied in 1 cubic centimetre ampoules each containing 10 milligrams of the naphthoquinone derivative for intravenous injection, and in 10-milligram tablets for oral administration. The ready solubility of synkavit in water considerably enhances its value in treatment, since it may be given by mouth with the same effect as other naphthoquinone analogues which are administered by injection. Toxic effects have not been encountered with any of the above preparations in the doses stated, but kapilon given intramuscularly may cause pain at the site of injection.

Preventive treatment

Haemorrhage in jaundice may be prevented by raising and maintaining the blood prothrombin at or near the normal level. This may be achieved by giving 2, 10-milligram tablets of synkavit by mouth or by injecting 2, 5-milligram ampoules of kapilon intramuscularly every week. In preparing a jaundiced patient for operation, 2, 10-

milligram tablets of synkavit are given by mouth 3 days before operation, on the day of operation, and on the third day after operation, or 2, 5-milligram ampoules of kapilon may be substituted for the synkavit and injected intramuscularly at the same time

Curative treatment

In the treatment of haemorrhage resulting from prothrombin deficiency, 1-3 cubic centimetres of hykinone or 1 cubic centimetre of synkavit is injected intravenously. On the next day 2, 10-milligram tablets of synkavit are again given by mouth and thereafter a normal blood prothrombin level is maintained by repeating this dose every week. If there is no increase in the blood prothrombin 6 hours after the initial injection the only other effective method of raising it is to transfuse 1-1½ pints of fresh blood. The increase in the blood prothrombin achieved by transfusion is

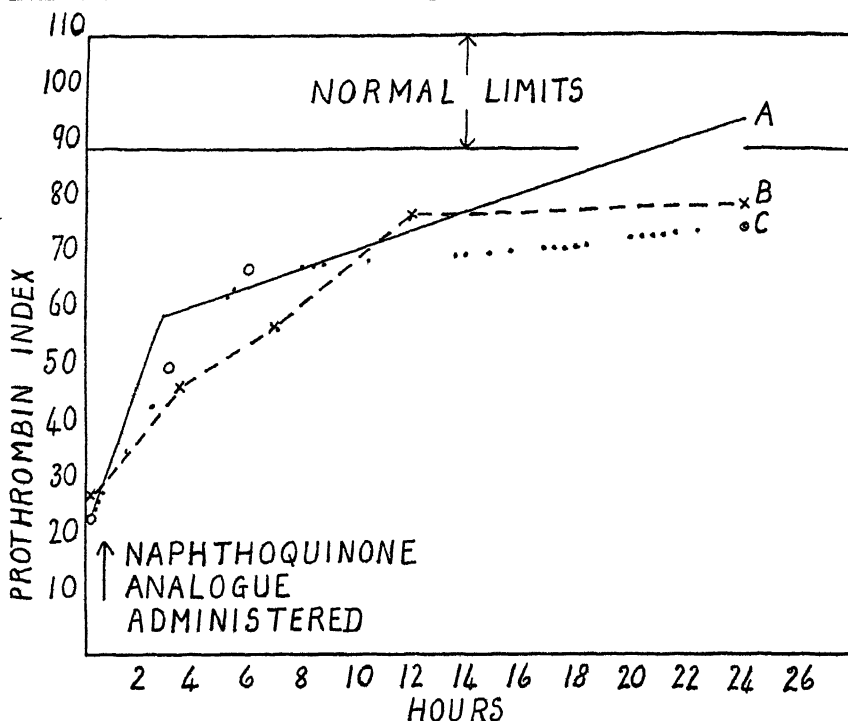


FIG 2—The effect of naphthoquinone analogues on the prothrombin index of three jaundiced patients with carcinoma of the head of the pancreas A=10 milligrams synkavit injected intravenously B=10 milligrams kapilon injected intramuscularly C=20 milligrams synkavit by mouth (Reid)

moderate and temporary but it may be sufficient to arrest the haemorrhage. The effect of intramuscular injection of 10 milligrams of kapilon, intravenous injection of 10 milligrams of synkavit, and oral administration of 20 milligrams of synkavit on the blood prothrombin level of 3 jaundiced patients with carcinoma at the head of the pancreas is shown in Fig. 2. The blood prothrombin level is assessed by determining the coagulation time of a sample of blood in which all the necessary constituents for coagulation, except prothrombin, are known to be present in sufficient quantities. This coagulation time has been termed 'the prothrombin time' since the time taken for coagulation is inversely proportionate to the amount of prothrombin in the blood. The normal prothrombin time varies within narrow limits and, in order that results may be compared from day to day, the blood prothrombin level is expressed as 'the prothrombin index' (Quick, Stanley-Brown and Barcroft) which is determined as follows:

$$\text{Prothrombin index} = \frac{\text{Normal control prothrombin time in seconds}}{\text{Unknown prothrombin time in seconds}} \times \frac{100}{1}$$

The prothrombin index is thus expressed as a percentage of normal and the range in health is 90-110 per cent.

Almquist, H. J., and Klose, A. A. (1939) *J. Amer. chem. Soc.*, **61**, 1923

Ansbacher, S., and Fernholz, E. (1939) *J. Amer. chem. Soc.*, **61**, 1924

JOINTS, INJURIES AND INTERNAL DERANGEMENTS—KALA-AZAR

- Binkley, S B, Cheney, L C, Holcomb, W F, McKee, R W, Thayer, S A, MacCorquodale, D W, and Doisy, E A (1939) *J Amer chem Soc*, **61**, 2558
Brinkhous, K M (1940) *Medicine, Baltimore*, **19**, 329
Fieser, L F, Campbell, W P, Fry, E M, and Gates, M D, Jun (1939) *J Amer chem Soc*, **61**, 2559
Kark, R, and Souter, A W (1940) *Lancet*, **1**, 1149
Macfie, J M, Bacharach, A L, and Chance, M R A (1939) *Brit med J*, **2**, 1220
McKee, R W, Binkley, S B, Thayer, S A, MacCorquodale, D W, and Doisy, E A (1939) *J biol Chem*, **131**, 327
Manson-Bahr, P (1943) *Practitioner*, **150**, 265
Quick, A J, Stanley-Brown, M, and Barcroft, F W (1935) *Amer J med Sci*, **190**, 501
Reid, J (1941) *Brit med J*, **1**, 579
Stein, H B (1942) *S Afr med J*, **16**, 12

JOINTS, INJURIES AND INTERNAL DERANGEMENTS TRAUMATIC DERANGEMENT OF JOINTS

The knee-joint

Traumatic derangement of semilunar cartilages

Treatment—MacAusland states that arthritic changes or associated pathology in the knee-joint may lead to non-success at operation or at least to a result which is not the best. A very important aetiological factor is persistent weakness of the quadriceps extensor muscle. Prompt and effective treatment of derangements of the cartilages is a safeguard against the development of other changes in the joint at a future date. Furthermore, by having early treatment the patient is able to concentrate on the development of better tone in the quadriceps muscle. MacAusland's experience extends for over 30 years and he refers to 850 cases of derangement of the semilunar cartilage. In his series of cases 90 per cent of the patients were clinically improved.

MacAusland, W R (1943) *Surg Gynec Obstet*, **77**, 141

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KALA-AZAR

MORPHOLOGY AND LIFE-CYCLE OF *LEISHMANIA DONOVANI*

Transmission

The outstanding event in tropical medicine during 1942 was that the final proof was provided that the infection of kala-azar is conveyed to human beings through the bites of *Phlebotomus argentipes*, this has been established nearly 40 years after the human stage of *Leishmania donovani* was discovered. Success has at length been obtained in 5 consecutive feeding experiments on Khasia Hill men in Shillong who had not resided in a kala-azar infected area, the experiments were carried out by Swaminath, Shortt and Anderson who adopted the simple technical modification of keeping alive *P. argentipes* organisms fed on kala-azar patients by subsequently feeding them on raisins instead of giving them blood feeds. Repeated feeds on the Khasias were given over from 3 to 5 months before the men were shown to be infected, so that the precise incubation period of the disease is not settled. The authors suggest that their success may have been due in part to the fact that the sand-flies were fed on patients with the epidemic form of the disease met with during a recrudescence in Assam, they think this may have resulted in increased virulence of the parasite.

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TREATMENT

Antimony compounds

Sati advises the alternate use, for a week at a time, of tartar emetic and a pentavalent antimony compound with which he obtained favourable results. The beneficial effects of the use of stilbamidine (4'-diamidinostilbene) in cases of kala-azar have been confirmed by Napier, Sen Gupta and Sen, who conclude, from experience of 100 cases, that the introduction of this preparation is a very great advance even on the use of neostibosan, moreover, patients who are antimony-resistant respond to it. The dosage the above workers finally adopted was an initial dose of 0.025 gramme, increased by 0.012 gramme at a time, up to a maximum of 0.001 gramme per pound of body weight. Reactions in the form of unpleasant sensations and of low blood pressure are controlled by a previous injection of adrenaline, and are not dangerous. Although many of the patients were in an advanced state of the disease, only 2 per cent died and another 2 per cent relapsed. Fulton and Yorke found increased toxicity in old solutions of stilbamidine, and therefore they advise that only freshly made solutions should be used.

- Fulton, J D, and Yorke, W (1942) *Ann trop Med Parasit*, **36**, 14
Napier, L E, Sen Gupta, P C, and Sen, G N (1942) *Indian med Gaz*, **77**, 321

Sati, M H (1942) *Ann trop Med Parasit*, **36**, 1
Swaminath, C S, Shortt, H E, and Anderson, L A P (1942)
Indian J med Res, **30**, 473

KIDNEY, SURGICAL DISEASES

MOVABLE KIDNEY

Diagnosis and differential diagnosis

- 832 Hess advises that pyelograms should be taken during full expiration and full inspiration on the same film ('respiration pyelography') to measure the amount of mobility of the kidney. After operations for the fixation of the kidney they were of value in estimating the results.

CALCULI

Aetiology

Effect of prophylaxis

- 834 Sulphapyridine, sulphathiazole and sulphadiazine are the three most common representatives of the sulphonamides used, and it has been established beyond doubt that unless certain precautions are taken haematuria and anuria may result if the therapy is not carefully supervised. The cause of the haematuria is a deposition of the crystals of the acetylated compounds in the renal tract, this phenomenon occurs only in urine which is above the average specific gravity (1014). If the amount of urine passed in 24 hours is below 1,500 cubic centimetres, haematuria is thus to be expected and should be anticipated, especially in hot climates. Anuria is the last stage and often ends in death, it is associated with impairment of renal function and nitrogen retention. The main symptom is pain, most severe in the suprapubic and lumbar regions.

Treatment

Haematuria and anuria in sulphonamide therapy

The prevention of crystallization of the sulphonamide drugs is not a mere matter of rendering the urine alkaline, and there is ample evidence in the literature that haematuria may develop in patients who have an alkaline urine and are already on a course of alkaline treatment. The best insurance against anuria is to see that the patient has at least 5 pints of fluid every day, this will result in a secretion of at least 1,500 cubic centimetres, and the giving of full doses of sulphonamides need not be interfered with. So far as the actual condition of anuria is concerned, catheterization and washing out of the ureter are essential. If there has been anuria for more than 12 hours operation is indicated, this generally taking the form of cystoscopic examination, followed by catheterization of the ureter and on each side washing out of the pelvis of the kidney. Sometimes it is necessary to perform unilateral nephrostomy. It almost goes without saying that if the anuria has been going on for a few hours fluids should be limited, for if there is complete occlusion of the ureter there will be danger of hydronephrosis and congestion of the capillaries.

Flynn has reported that in the early stages of anuria massage over the kidney regions and ureters externally, and the lower end of the ureters per rectum, has been successful, in certain cases intravenous infusion of physiological saline has been necessary.

PYONEPHROSIS

- 835 Roche¹ draws attention to the very great risk of heart failure involved in the operation of nephrectomy for pyonephrosis. This risk is quite apart from the technical difficulties due to dense adhesions present, and is the result of prolonged toxic absorption from the pyonephrosis on the heart which is unable to stand the strain of an operation. He quotes 2 cases of nephrectomy for calculous pyonephrosis, of which one patient died soon after the operation and the other during the operation. In one the right ventricle was found to be very thin walled and the unaided eye could see white fibrous sheaths in the heart muscle. The other patient was an ill-nourished youth with fatty change in the heart.

TUMOURS

- 840 Primary malignant tumours of the kidney in infants and in children have been reviewed by Campbell. He found records of only 2 cases of carcinoma in children, hypernephroma accounted for from 2 to 11 per cent, but by far the commonest was the Wilms's tumour (embryonal adenomyosarcoma). Tumours of the renal fibrous capsule and of the renal pelvis were extremely rare. The mortality in cases of renal tumour treated by nephrectomy was about 95 per cent. Campbell considered that the only way to reduce this figure is the use of intensive pre-operative and post-operative radiotherapy.

In 3 cases of adeno-carcinoma of the kidney and in one case of hypernephroma of the known duration of over 5 years Roche² noted the presence of calcification in the tumour. The calcification was visible in plain skiagrams. He suggests that it

may be a feature in the diagnosis of renal neoplasms, and is of the view that it may signify chronicity and low malignancy

In support Roche quotes a case, recorded by Grant, of calcified hypernephroma of the right kidney, of 8 years' known duration, Grant concludes that 'calcification in itself, apart from any other features present in the growth, is likely, therefore, to be of favourable significance'

Campbell, M F (1937) *J Amer med Ass*, 109, 1606

Flynn, W A (1943) *Lancet*, 1, 648

Grant, H M (1941) *Proc R Soc Med*, 35, 23

Hess, E (1938) *J Amer med Ass*, 110, 1818

Roche, A E (1940)¹ *Urol cutan Rev*, 44, 69

— (1941)² *W Lond med J*, 46, 20

LABOUR. I—NORMAL LABOUR

Corrigenda

In Vol VII, p 439, lines 17 and 18 the words 'or 1 in 1,000 mercuric chloride' should be deleted

On p 444 the last sentence should read 'The child is then weighed, dressed, and placed in a warm cot, with the head lowered to overcome cerebral anoxaemia'

FACTORS IN LABOUR

The passages

The female bony pelvis

Young summarizes the subject and states that the relaxation and mobilization of the pelvic joints in pregnancy have been shown within recent years to play a very minor part only during labour, and he advances evidence to show that the claims made for the Walcher position rest on a doubtful basis

The clinical states caused by excursive relaxation and mobility of the sacro-iliac joints are discussed and the group with excessive pubic mobility was found to be only 0.75 per cent in 4,512 persons examined. In sacro-iliac relaxation combined with the pubic lesion, in 46.7 per cent of women chronic backache developed, and in 25 persons forcible manipulations resulted in 68 per cent receiving complete relief

Young, J (1940) *J Obstet Gynaec*, 47, 493

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LABOUR III.—MALPOSITION AND MALPRESENTATION OF THE HEAD

Corrigenda

In Vol VII, p 453, for the first sentence in the paragraph on *Mechanism*, read

The occiput is usually primarily posterior, and one of three events may happen (1) either it rotates backwards through an eighth of a circle and is born as a persistent occipito-posterior, or (2) it rotates forwards through three-eighths of a circle and is born as an occipito-anterior position, the latter is the more usual, or (3) occasionally the head is arrested in the transverse diameter during rotation from the posterior to the anterior position

On p 454, under *Diagnosis*, for the sentence beginning 'By abdominal palpation' read 'By abdominal palpation at the beginning of labour it is not difficult, as a rule, to diagnose occipito-posterior positions, but in the later stages of labour a vaginal examination will probably be necessary'

On p 455, in the paragraph on *Vaginal examination*, the first sentence should read 'It is usually necessary to make a vaginal examination to confirm the palpation diagnosis of occipito-posterior positions'

On p 459, for the marginal title '*Ballottement*', read '*Non-fixation of the head*'

On p 460, line 17, for '*ballottement*' substitute '*non-fixation*'

On p 462, in line 2 of the paragraph on *Movement of the head*, for 'child' read 'chin'

On p 466, line 4, at the end of the 2nd sentence, ending 'by this method', add 'but it is seldom necessary'

On p 466, line 25, delete remainder of paragraph after sentence which ends 'on the breech'

Addendum

On p 457, add at the end of the paragraph on *Forceps* 'The Kielland forceps are used by some obstetricians. The author of this article has never found it necessary to use them'

The double application of the forceps which was originally described by Smellie, and later brought to notice by Scanzoni (the Scanzoni procedure), gives excellent results when the occiput cannot be rotated manually from its oblique posterior position

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Treatment

The acute laryngo-tracheo-bronchitis seen in children may be a very serious disease, worse than croupous diphtheria. Of 4 patients 3 died and the patient who survived, a boy 9 months of age, was treated by the administration of 6 grammes of sulphapyridine. Improved statistics may therefore be expected when chemotherapy has had more extensive use (Fabritius).

TUMOURS OF THE LARYNX

Malignant

According to Colledge the application of radiotherapy to the laryngeal and pharyngeal regions for carcinoma has not been justified. In a table published by the Medical Research Council only 8 out of 285 patients so treated show a 5-year result and no 10-year results. Further, the method is seldom successful and causes much suffering and loss of life. Operation figures for the same condition (153 patients operated on between 1920 and 1935) showed the following results: 76 remained well for over 5 years, 34 had no recurrence for more than 10 years, of the latter cases 27 were of intrinsic cancer of the larynx and 7 were extrinsic.

Quick, discussing the treatment of intrinsic carcinoma of the larynx, states that there is a very good chance of cure by X-irradiation in cases which are not complicated by previous treatment, that there is not any interim risk, and that a complete restoration of function is obtained. Radium should not be used in early favourable cases, but may be of value in conjunction with laryngofissure in advanced cases, in cases which are resistant to X-irradiation, and in recurrences.

Colledge, L. (1940) *Brit med J*, **1**, 784

Fabritius, H. F. (1943) *Acta oto-laryng*, *Stockh*, **31**, 348

Jackson, C. (1937) *The Larynx and Its Diseases*, p. 110. Philadelphia and London

Quick, D. (1941) *Amer J Roentgenol*, **46**, 11

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LEAD POISONING

AETIOLOGY

Corrigendum

In Vol VII, p. 658, for the paragraph on *Notification*, substitute the following:

The widespread use of lead in industry accounts for practically all the known cases of lead poisoning in Great Britain. The disease, if it occurs in a factory, is, by Section 66 of the Factories Act, 1937, compulsorily notifiable by medical practitioners to the Chief Inspector of Factories, Home Office, Whitehall, S.W. 1, if affecting a person employed in the painting of buildings; the disease must similarly be notified under Section 3 of the Lead Paint (Protection against Poisoning) Act of 1926.

LEISHMANIASIS, CUTANEOUS

ORIENTAL SORE

Treatment

Cure

Local—Holmes reports on the mass treatment of oriental sore amongst the troops who helped to clear the debris at Quetta; he, with most of his colleagues, preferred surgical measures with or without the intravenous injection of the trivalent antimony compounds, and reported poor results with the pentavalent compounds. The best results have been obtained when the sores have been scraped under an anaesthetic, treated with liquid phenol, and then have had Elastoplast applied for 14 days without removal.

Hamburger pointed out that not all sores occurring on the North-West Frontier in India are due to *Leishmania*, this may account for the disparity in the reports on the result of treatment in oriental sore diagnosed clinically, which are still unfortunately the rule. Manson-Bahr recommended the following paint for oriental sores:

Cignolin	—	—	—	—	60 grains
Ichthammol	—	—	—	—	120 grains
Oil of cade	—	—	—	—	40 minims
Rectified benzene to	—	—	—	—	1 ounce

and for more chronic sores a similar ointment:

Cignolin	—	—	—	—	60 grains
Zinc oxide	—	—	—	—	240 grains
Olive oil	—	—	—	—	240 minims

SOUTH AMERICAN CUTANEOUS LEISHMANIASIS

Aetiology

This disease appeared in epidemic form during the war in the Chaco district of Paraguay. Infection of the lymphatic glands occurred in 12 per cent of the cases.

933

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Hamburger, H J (1939) *Indian med Gaz*, **74**, 151
Holmes, F (1937) *J R Army med Cps*, **69**, 258
Manson-Bahr, P (1937) *Festschrift Bernhard Nocht zum 80 Geburtstag von seinen Freunden und Schülern*, p 278 Hamburg

LEPROSY

AETIOLOGY

Age incidence

In Brazil

935

De Souza Araujo and de Albuquerque found that in Rio de Janeiro, among native Brazilians, 37.9 per cent of leprosy patients were under 20 years of age, 52.2 per cent were between 21 and 50 and 9.8 per cent were over 50 years, in foreigners the respective figures were 5.0 per cent, 62.2 per cent and 32.7 per cent, so that 94.9 per cent of the latter were attacked after the age of 20 years. Thus grown-up European immigrants are as susceptible as Brazilian children are. Brazilians born there of foreigners showed an age incidence similar to that of pure native Brazilians, so that the susceptibility of immigrant foreigners appears to be related to their having been brought up in countries free or nearly free of leprosy.

Geographical incidence

In Nigeria

Davey² reports on the progress of untreated cases of leprosy, as revealed by a second survey after an interval of 2 years in south-eastern Nigeria. The incidence at a second visit was raised from 6 per cent to 6.7 per cent by finding some new cases, but 2 years later the figure had fallen to 5.7 per cent, apparently as the result of village segregation, in spite of the development of 10 new cases. Deaths had amounted to 18, 6 of them from smallpox. One-third of the number of patients were worse and two-thirds were stationary or improved. In all the infectious cases the patients have now been accommodated in the model leper village built by themselves with the cordial help of the chiefs, and regular treatment is being provided, a further contemplated survey in 2 years' time should be of interest.

In Great Britain

Rogers, Cook and Muir report the results of inquiries made from British dermatologists about the number of cases of leprosy seen in Great Britain in the last three or four decades. The total number reported was 87, of whom 23 were dead, 13 had been repatriated, and 11 had not been seen for more than 10 years, so were probably either dead or repatriated. Of the remaining 40, including 8 last seen within 10 years, only 22 were of the infective lepromatous type, and all but 4 not seen recently were under care in a home or under skilled treatment, and so are unlikely to be a danger to the healthy. They advise that the very few cases not under effective care should be accommodated at the Homes of St. Giles.

In Ceylon

De Simon reports on the progress in Ceylon, since in 1832 sole reliance on compulsory segregation gave place to modern methods. Surveys and propaganda and training medical officers in early diagnosis have led to the establishment of out-patient clinics for uninfected patients, and repeated examinations are made of contacts and discharged persons. The number of cases known in 1939 was 3,648, of which 2,548 were found by the surveys, and modern treatment is expected to restore to health the majority of patients in the early cases and to reduce the number of the infective ones. Surveys showed that 85 per cent of cases were within five miles of the humid coast.

In the Belgian Congo

From a leprosy survey in the humid tropical Nepoko District of the Belgian Congo, Degotte points out the very high rate of 5.29 per cent, but the infective lepromatous cases formed only 6.61 per cent of the total. It is important to note that in 43 per cent of the foci the appearance of lepromatous cases was soon followed by an extension of the disease. Segregation is advised, for in areas with relatively good village isolation the cases were only one-third as numerous as under the contrary conditions.

In Bengal

Lowe, Dharmendra and Sen record the results of a re-survey, after 4 years, of a rural district of Bengal in which effective measures had not been taken during that period. No material change had taken place in the total number of cases but the lepromatous cases in children had increased. Of the original 424 cases, 59 patients had died, including a large proportion of lepromatous ones. In 44 new neural cases 11 patients had shown suspicious lesions 4 years earlier. In 80 per cent of the new cases there had been contact with an infective case and 41 of 56 new cases were found in families in which previous cases had been recorded. Of 328 neural cases, all those of children living in contact with infective cases, only 2 had become lepromatous and 61 per cent of the new cases originated in early life. The importance of protecting children is obvious.

In Canton

Rai reports a leprosy survey in Canton in which 52,000 persons were examined and 84 cases, 1.6 per thousand, were found, mostly neural ones. This is a lower rate than the estimates of others show, so the usual assumption that there are one million leprosy patients in China may prove to be an overestimation.

In the West Indies region

Muir¹ has recorded important data regarding leprosy in the West Indies region obtained at inspection visits and surveys, together with recommendations for the control of the disease in this for the most part backward area. A partial survey of Trinidad and Tobago indicates the presence of about 1,000 cases of leprosy. As only cases of advanced leprosy are isolated at the Chacachare Island settlement the law should be amended in order to allow cases of early leprosy to be treated at clinics, school children should be examined so that the disease may be detected while it is still amenable to treatment. Jamaica is very backward, having 172 patients isolated in an overcrowded asylum, the authorities should adopt modern measures. The same is true regarding the island of Barbados and the other small British West Indian islands. British Guiana, as the result of 15 years' work by Dr F. G. Rose using modern treatment, combined with modification of the compulsory segregation law in order to permit patients in early stages of the disease to be treated at out-patient clinics, presents a pleasing contrast and is a good example to the West Indies. As the result of a relaxation of the compulsory segregation laws there are now 9 clinics at which 500 out of the total of 1,000 patients are being treated while still in an early uninfected stage and the more advanced infective patients are being cared for at the up-to-date leprosy colony at Mahaica. Here the value of regular and persistent modern treatment is shown by the fact that of the patients in that colony who have received 60 per cent and upwards of the prescribed course 71.4 per cent have had the disease arrested, whereas it has been arrested in only 16.7 per cent of those patients who received 60 per cent or less of the full course of treatment. Many formerly advanced lepromatous patients were found by Muir to have been freed from infection and from active symptoms over a number of years. He concluded that the decline in recent years in the notification of new cases of leprosy from between 40 and 100 to only 39 cases annually, is the result of an actual decrease of leprosy in the colony.

PATHOLOGY AND BACTERIOLOGY

Inoculation of rhesus monkey

Collier, and McKean report successful inoculation of 15 rhesus monkeys with leprosy. These experiments were begun by Oberdorffer in the Mission Leprosarium at Chiangmai, Siam, and continued by the authors after he left. After feeding with colocasia for some 2 months, leproma was inserted under the skin of the back. The following symptoms were noted after 17 months: positive ear clips, positive nasal smears, depigmentation, deep red coloration of areas of the face with induration and nodules, thickening of the ulnar nerves, nodules forming at a distance from the original inoculation, abscess at a distance with acid-fast bacilli as the only organism found, hypertrophy of the nipples with bright red colouring and loss of hair. Material taken from a nodule of one monkey and inoculated into another produced positive results more rapidly than in the original animals. Control monkeys on ordinary diet gave negative results, as did also monkeys fed on colocasia but not inoculated with leprosy. When monkeys, instead of being fed on colocasia, were inoculated with sapotoxins extracted from colocasia, results were more rapid.

Animal infections

The failure of Dharmendra and Lowe to infect hamsters with human leprosy bacilli shows that those animals are not likely to be of much value for chemotherapeutic experiments with a view to discovering more active drugs against leprosy. More promising in this connexion is the recent success of Ota and Nitto in the infection of hens, which were the most suitable of various animals with which they experimented. They used for injection 0.5 grain of the deposit of human lepromas together with their standard rice mixture, and obtained positive results. More extensive lesions were produced by adding to the 0.5 grain leproma deposit in 5 cubic centimetres of physiological salt solution, 0.05 kieselguhr, trypan blue and potassium iodide, and injection of the whole deeply into the small pectoral muscles, with a control injection of the leprous material alone into the other side. After 3 or 4 months the control injection was absorbed, but the infected muscle of the other side showed yellow dots and lines fairly closely distributed in which a very rich accumulation of acid-fast bacilli could be demonstrated. These lesions persisted for more than a year and even slowly increased. The bacilli did not infect guinea-pigs and could not be cultivated, so were not *Bacillus tuberculosis*. Large vacuolated cells containing acid-fast bacilli were found, and successful passages were made through a series of 7 birds. If these results are confirmed they promise to be of great practical importance.

Systemic disease

Fite has studied the vascular lesions in 77 cases and in 10 necropsies. He concludes that leprosy foci apparently originate in the perivascular lymphatic spaces around arteries, veins and nerves, the bacilli are probably discharged continuously from the endothelial cells into the circulation in lepromatous cases, they were also demonstrated in the liver and spleen.

CLINICAL PICTURE

Types of lesion

Muir³ found in the Pretoria Leprosy Institute that leprosy was of a more severe type among the European patients than among the Bantus, almost all the former having the severe lepromatous type, whereas among the natives there, as in most parts of Africa, the percentage of this type is approximately 25. It is generally acknowledged that the lepromatous type is associated with low resistance to the disease. It would therefore appear as if the resistance of Europeans to leprosy is less than that of the dark-skinned races of Africa. This is supported by similar findings in Europe, where in Cyprus, Malta and elsewhere most cases are of the lepromatous type. These findings do not support the theory that natural selection is the dominating influence in determining the present freedom of Europe from leprosy.

In children

The earliest signs of leprosy in children have been studied in 975 cases by Araujo in the Rio de Janeiro leprosarium. In 38.7 per cent they were maculae and in 27.2 per cent dysaesthesiae. They were distributed on the face, arm, leg, buttock and thigh, and were most numerous on the lower extremity. Contact with a leprosy patient might thus be the cause of infection.

Effect of vaccination

Archer records a good example of leprosy reactions following vaccination against smallpox at the Purulia Leper Home, India. Owing to the development of smallpox by a patient the 900 inmates were vaccinated. In the fortnight before this leprosy reactions had been noted in only 11 of the leprosy patients, but in the fortnight after the vaccination there were 41 reactions of a more severe type than usual, all in patients in whom vaccination had been successful.

Eyes

Eye lesions

Prendergast reports a careful study of the eye lesions of leprosy, made at the United States of America leprosarium. The cornea is the most commonly affected tissue, the iris and ciliary body show localized lesions, but the nerve layer and lens are rarely involved. Quinine bisulphate ointment and thyroxin used locally were fairly effective in corneal lesions, and protein shock therapy gave good results in acute lesions. Surgical measures are not well tolerated. Protection of the eyes is an important prophylactic measure.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Lepromin test

Important advances have been made, more particularly in prognosis, in the technique and results of the lepromin reaction. It is generally agreed that the injection of sterile emulsions of leprosy nodules containing both the bacilli and the tissue cells produces a typical late nodular reaction, often resulting in ulceration, in mild neural and in tuberculoid leprosy, but negative reactions in lepromatous cases with bad prognosis. In addition an early congestive reaction is commonly noted in patients showing a positive reaction. Investigations in the Calcutta School of Tropical Medicine by Dharmendra and Lowe have been made with the purpose of isolating a pure antigen, it was found that on separating the lepra bacilli from the tissue cells by the repeated centrifugalization, and grinding up of the bacilli in order to free their contents, the injections produced much earlier distinct reactions and greatly diminished late reaction. Further fractionation by chemical means showed that the specific substance resided solely in the protein fraction, which produced very little late reaction with no ulceration, thus having the further advantage of a much earlier reading. Fernandez and Castro have confirmed these observations, obtaining similar results by using as an antigen emulsions of ground-up leprosy nodules so filtered through an L3 candle as to contain only soluble products. In these ways early and reliable results which are of value in prognosis can be obtained by the test. On repeating the test every month and using up to from 5 to 15 injections, Dharmendra, Lowe and Mukherji were unable to confirm an earlier statement of Borgehr that negative can be converted into positive reactions, so the injections do not appear to increase the power of resistance in patients.

Lowe and Dharmendra have recorded observations contributing to our knowledge of the technique and value of this test. To prepare the lepromin they autoclaved leprosy nodules and ground up and repeatedly centrifuged the material to remove tissue cells, the supernatant fluid containing the organisms is diluted to contain 15 millions per cubic centimetre and 0.1 cubic centimetre of this is

used A study of the early and late reactions with this material shows that both were obtained in 85 per cent of 300 tests and in only 6.7 per cent did the results differ With the separated ground bacilli the early local reaction at the site of injection was accelerated by 24 hours and late reactions were reduced in degree They therefore think the early reaction is produced by broken-down bacilli Further work on fractionation of lepromin showed that the protein content of the bacilli is responsible for the reaction A sixth contribution reports the results of the test in 660 cases, with readings up to the sixth week Patients classed as negative did not show any reaction or only slight induration of from 3 to 4 millimetres in diameter, weak positive reactions showed induration of 3-4½ millimetres, and definitely positive ones showed nodules of from 5 to 7 millimetres diameter and upwards, often with ulceration Lepromatous cases gave 90 per cent negative results and 10 per cent weak positives, neural cases gave from 6 per cent to 22 per cent negative, from 19 per cent to 35 per cent weak positive and from 43 to 75 per cent positive reactions Anaesthetic and tuberculoid neural cases gave the highest proportion of positive reactions The presence of leprosy bacilli in the lesions is associated with more negative or weakly positive reactions, so the lepromin test is of some prognostic value

In children

Cochrane, Rajagopalan, Santra and Raj report on the lepromin test in children, they conclude that the lepromin reaction tends more often to be negative in children in whom a history of contact with leprosy cases is maximal, but it is not significantly influenced by hereditary disposition Continuous contact with an open case is the most important factor in breaking down resistance to infection

TREATMENT

Prophylactic

General

Contacts —Nigeria affords a further example of the success of modern methods of dealing with the leprosy problem Briercliffe estimates the leprosy cases in Nigeria at some 200,000 or at least 10 per thousand of the population The Government grant of £5,000 a year, supplemented by the British Empire Leprosy Relief Association, has provided 14 settlements in the 23 provinces The success of the voluntary system of segregation is evidenced by the increase of the inmates from 2,500, 10 years ago, to nearly 7,000, the increase being limited only by lack of funds Davey¹ records the success of prophylactic measures around the Uzuakold leper colony in the Owerri Province of Southern Nigeria A survey in 1939 revealed an incidence of 33 per thousand among 11,689 persons examined Leper villages for the isolation of infective cases and clinics for the weekly treatment of earlier ones were supplied and at the end of the year, 1,243 cases were being treated with rapidly increasing numbers at a very low cost An unpublished report received in 1941 recorded that the clinics had been increased from 4 to 6, and the registers showed 10,000 cases, for the injection of which several pints of hydnocarpus oil were being used every week

Curative

General

Diet —Concepcion and Camara report that estimations of ascorbic acid in the blood in 96 cases of leprosy showed it to be reduced in the plasma in more or less direct proportion to the severity of the cases The normal level was restored by the intramuscular injection of 50 milligrams

Special

Leprosy reactions —In the treatment of leprosy reactions Cochrane, and Germond advise antimony given intramuscularly in the form of foudadin Germond claims even better results with soluseptasine given intramuscularly or intra-arterially Ryrie recommends for leprosy ulcers dressings containing vitamin A in the form of cod-liver oil, red palm oil, minced goat's liver and especially shark-liver oil For lepromatous ulcers Muir² strongly recommends a modification of the treatment of burns with nitrate, tannic acid and gentian violet

Muir found a surprisingly large number of lepromatous ulcers as compared with trophic ones They took up much time in dressing, but this was greatly reduced by the following method The ulcers were first painted with a 1 per cent solution of gentian violet or methyl violet in alcohol, then with a 10 per cent watery solution of tannic acid 3 or 4 times on the first day, and later once a day The ulcers rapidly began to heal, greatly to the comfort of the patients

Araujo, H C de S (1940) *Brazil-med*, 54, 145

— and de Albuquerque, A F R (1940) *Ata Medica*, 6, 63

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Cochrane, R G (1940) *Int J Leprosy*, 8, 445

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 — (1941)² *Int J Leprosy*, **9**, 77
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 — and Lowe, J (1940) *Indian J med Res*, **28**, 61
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 — — (1942) *Indian J med Res*, **30**, 1, 9 and 17
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 — (1942)² *Leprosy Rev*, **13**, 22
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 de Simon, D S (1940) *J Ceylon Br Brit med Ass*, **37**, 171

LEUCODERMIA

PHYSIOLOGY OF PRODUCTION OF MELANIN

Formation in body

936

Most authorities are agreed that all cutaneous pigment is laid down in the epidermis and not conveyed to it from the blood stream or elsewhere, but opinions are still at variance regarding the precise histological and biochemical mechanisms involved and the exact sites at which this formation takes place. Discovery of the origin and function of the dendritic cells and of the so-called dopa reaction by Bloch in 1917 (see Vol VII, p 706) have greatly helped to elucidate this problem. Meirowsky asserts that the dopa reaction 'is positive in all mammals wherever pigment is produced, with the exception of the superficial corium cells and those cells in which melanogenesis is complete'.

More recent work, however, has modified the view that the dopa reaction is specific. Thus Schaaf has shown that extracts of the skin will oxidize not only dopa but catechol, hydroquinone, *d*-3-dioxyphenylalanine, and sometimes even *p*-cresol, thus suggesting 'that the melanogenic enzyme of mammals is a polyphenol oxidase' (Meirowsky²). The same writer is now inclined to the view that the formation of pigment is brought about not by enzymes but by catalysts of a quinone-like character. He points out that such bodies are related to tyrosine which, together with adrenaline or its oxidation products, may be important as forerunners of melanin. The central problem, however, is the origin and significance of the dendritic cells, which lie characteristically in the basal layer of the epidermis and play an important part in the manufacture of pigment in the response both to normal physiological stimuli, for example the sun, and to pathological processes, for example in Addison's disease and arsenical pigmentation.

Masson, and Pautrier, Lévy and Diss, regarded these dendritic cells as morphologically and genetically derived from the nervous system, but Bloch, using his dopa method, showed that pigment-forming cells looked like ordinary cubic epithelial cells when stained by the usual methods and like dendritic cells when his special procedure was adopted. Meirowsky concludes that the dendritic cells have not immigrated from the corium and are not nerve cells but modified epithelial cells. He also asserts that the dendritic cell is not the only source of melanin. The pigment can be manufactured independently in the cells of the Malpighian layer, as he claims to have proved by irradiation experiments on the non-pigmented skin of dark subjects. Finally, he believes that the dendritic cells may have developed from the undifferentiated epidermis 'as a special system', in the same way as the hairs, nails and glands, or as the Langerhans cells from the ordinary cells of the pancreas. Meirowsky concludes with a discussion on the morphological forerunners of melanin, in his view (Meirowsky^{1 2}) this is always derived from the nucleus and not from the cytoplasm of the participating cell. Wherever melanogenesis

takes place it is preceded within the nucleus by an increase in that substance which is stained red by the Unna-Pappenheim method 'All shades from the red substance to the very dark pigment can be shown, and in precipitate melanogenesis sometimes the whole nucleus or the nucleoli are transformed into melanin.'

A leading article in the *British Medical Journal* quotes a report by Schwartz, Oliver and Warren of an occupational leucodermia due to an ingredient in the rubber of gloves worn by negro and white workers in tanneries in the United States of America. The condition was in some cases preceded by itching and mild dermatitis, but there was no great discomfort or disability. Localization of the lesion to the hands generally led to an investigation of the gloves, which were identified as 'acid cured' gloves, in these the rubber mix had recently been modified by the addition of 0.2 per cent of an antioxidant—the monobenzyl ether of hydroquinone—not previously used. In negroes the areas of depigmented skin were a flat white, but in white workers the leucodermia showed only in summer when the skin of the glove areas failed to tan. Not in any case were the hairs bleached. Re-pigmentation gradually occurs if there is no further contact with the antioxidant. It seems that the action of the monobenzyl ether of hydroquinone in the skin is similar to its action in rubber, that is, it prevents the oxidation of the unsaturated linkages in the rubber molecule, and the oxidation of the propigment (dopa) in the skin.

Experiments by Figge on the oxidation of dopa by tyrosinase and by atmospheric oxygen suggest that positive dopa reactions may be due to the pressure in the skin of certain reversible oxidizable substances which facilitate the oxidation of dopa.

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 Masson, P (1926) *Ann Anat path med-chir*, 3, 417, 657
 Meirowsky, E (1909)¹ *Origin of Melanotic Pigment* Leipzig
 — (1933)² *Handbuch der Haut- und Geschlechtskrankheiten* (Jadassohn, J.), Berlin, 4, 588
 — (1940)³ *Brit J Derm*, 52, 205
 Pautrier, L M, Levy, G, and Diss, A (1928) *Arch Derm Syph, N Y*, 17, 1
 Schaaf, F (1938) *Arch Derm Syph, Wien*, 178, 535, 646
 Schwartz, L, Oliver, E A, and Warren, L H (1940) *Publ Hlth Rep, Wash*, 55, 1111

LEUCORRHOEA AND OTHER NON-HAEMORRHAGIC VAGINAL SECRETIONS

NORMAL VAGINAL SECRETION

After menopause

According to the observations of Wollner, ovarian hormone is capable of producing histological changes in the atrophic cervical mucosa of women after a physiological or artificial menopause. Hormonal stimulation by large doses of oestrogenic hormone can produce a hypertrophy of the columnar epithelium with hyperaemia, oedema, leucocytosis and desquamation—a condition found commonly in cases of endocervicitis. The administration of progestin stimulates the growth of the squamous epithelial elements. Further work may result in a hormonal cure being found for certain cases at present diagnosed as endocervicitis and erosion of the cervix.

937

LEUCORRHOEA

Treatment

The most important factor in the cure of vaginitis except that due to monilia is the maintenance of a low pH in the vagina. An acid reaction may be produced by oestrogen therapy by mouth, by vaginal suppositories or both, supplemented by the introduction into the vagina of an acid preparation.

939

Karnaky¹ published a list giving the pH of various substances used for douches. Except when the discharge is due to monilia the following should be avoided: sodium bicarbonate, sodium chloride, magnesium sulphate, iodine, potassium permanganate and borax.

Roblee and Karnaky have independently shown that the addition of acid fermentable material to the vagina, and maintenance of the pH at from 4 to 4.5, will cure most cases of cervical erosion.

Karnaky², continuing his investigation of the efficacy of various chemicals as douches, claims that the use of weak acetic acid (4 tablespoonfuls of 5 per cent acid to 2 quarts of water) is followed by more improvement in the flora than by the use of lactic acid.

Karnaky³ examined the husbands of 150 women in whom *Trichomonas vaginalis*

infection recurred, and found that 38 of them harboured the organism in the urethra, in the prostate or under the prepuce. Most had no complaints but a few had itching of the glans. The husbands in the series were instructed to use a protective covering for 3 months as the trichomonas usually die off spontaneously within 2 or 3 months. Hesseltine emphasizes the effectiveness of daily insertion of a 1-gramme tablet of lactose into the vagina in cases of vaginal trichomoniasis or senile vaginitis, claiming that the improvement in the flora is better than that produced by the insertion of oestrogenic hormone.

Successful results obtained by the use of negatan in cases of cervicitis have established it as a drug which is effective in cases in which cauterization cannot be carried out because of its dangers. Negatan, also known as negatol, is the condensation product of *m*-cresol sulphonic acid and formaldehyde, diluted with sufficient water to give a specific gravity of from 1.17 to 1.18. This substance possesses a strong coagulant action. The method of treatment used by Filler, Drezner and Adamo was as follows: Patients attended twice a week for treatment. After the vagina had been cleansed the eroded part of the cervix was painted with negatan and a gauze wick soaked in negatan was left in the cervical canal. A vaginal tampon was inserted to keep the wick in position, and the tampon was removed after 24 hours, when a vinegar douche was given. Sixty-five per cent of the patients were cured and 30 per cent were improved, there were 5 per cent failures.

Filler, W., Drezner, N., and Adamo, F. H. (1942) *Amer J Obstet Gynec*, **43**, 897

Hesseltine, H. C. (1939) *J Lancet*, **59**, 97

Karnaky, K. J. (1938) *1 Radiolog Rev*, **60**, 172, 208

— (1939) *2 Urol cutan Rev*, **42**, 633

— (1939) *3 Rad Rev Mississippi Valley med J*, **60**, 208

Roblee, M. A. (1938) *Amer J Obstet Gynec*, **35**, 1039

Wollner, A. (1939) *Amer J Obstet Gynec*, **37**, 947

LEUKAEMIA

THE LEUKAEMIAS ALL TYPES

Vol VIII Classification

940

It is believed that acute leukaemia is on the increase, relatively and absolutely there have been more cases of the acute form within recent years (Bethell). So far as treatment generally is concerned, X-ray therapy has given satisfactory results in both myelocytic and lymphocytic leukaemia. The treatment consisted generally of an intensive short course with exposure affecting the splenic area in cases of myelocytic and chronic myelomonocytic leukaemia. A current of 25 milliamperes of 200 kilovolts was used at a distance of 50 centimetres with copper and aluminium filters. Treatment may be given day after day. Care should be taken at the beginning to give small doses and to deal with limited fields.

MYELOCYTIC LEUKAEMIA

Chronic myelocytic leukaemia

Prognosis

941

In a study of 87 patients, the average duration of life after onset of symptoms was 3.2 years, 4 per cent of the patients survived for 10 or more years. Marked anaemia, relatively low leucocyte counts, and evidence of bleeding before beginning treatment indicate a short period of survival (Leavell).

CHRONIC SUBLEUKAEMIC MYELOSIS

947

A distinctive change in the radiographs in such cases is irregular density of the spongiosa of the long bones and throughout the flat bones, associated with decreased density of the corticalis of the long bones, the inner edge of the corticalis appearing frayed and irregular (Vaughan and Harrison). There may be increased erythrocyte thickness and fragility.

LYMPHOCYTIC LEUKAEMIA

Chronic lymphocytic leukaemia

Prognosis

948

The duration of life is shorter in patients who have marked anaemia and high leucocyte counts when first seen (Leavell). The occurrence of skin lesions does not affect the prognosis.

MONOCYTIC LEUKAEMIA

950

The value of supravital studies in doubtful cases of monocytic leukaemia has recently been emphasized (Beck). The young monocyte in a case of leukaemia may, unlike the normal mature monocyte, show no motility. The frequency of skin lesions, especially exfoliative dermatitis, in chronic as well as in acute monocytic leukaemia, has been described (Montgomery and Watkins).

LEUKAEMIA—LIPOIDOSES

PUNCTURE OF THE STERNAL MARROW

Marrow cells normal and in disease

Subleukaemic leukaemia

Scott considers puncture of the sternal marrow of particular value in subleukaemic lymphocytic leukaemia. The presence of more than 40 per cent of lymphocytes in the marrow suffices for a positive diagnosis. He doubts if a normal count excludes the condition.

955

In acholuric jaundice the marrow may be almost normal and it may contain an excess of normoblasts, erythroblasts and megaloblasts. The bone marrow in aplastic anaemia showed a variable state in Hynes's series. One case showed extreme hypoplasia, another marked hypoplasia, another moderate hypoplasia, while a fourth showed an active marrow with a normal differential count. Hynes considered sternal puncture to be inadequate for the diagnosis of aplastic anaemia. In other more obscure conditions, such as myelosclerosis and agranulocytosis, sternal puncture cannot be used for diagnosis and sternal biopsy is much more useful.

Beck, R. C. (1938) *Amer J clin Path*, 8, 509

Bethell, F. H. (1943) *Ann intern Med*, 18, 757

Hynes, M. (1939) *Lancet*, 1, 1373

Leavell, B. S. (1938) *Amer J med Sci*, 196, 329

Montgomery, H., and Watkins, C. H. (1938) *Minn Med*, 21, 636

Scott, R. B. (1939) *Quart J Med*, 8, 127

Vaughan, J. M., and Harrison, C. V. (1939) *J Path Bact*, 48, 339

LICHEN

LICHEN PLANUS

Aetiology

Statistics of female patients

Nervous strain, especially in the female sex, is a common predisposing factor in lichen planus, but sensitive conditions, chiefly of allergic type, may also give rise to the disease; it has been found also in association with alopecia, articular rheumatism and psoriasis. In a series described by Smith nearly all the women were over 50 years of age and the lichen planus affected the palms of the hands and the soles of the feet, other scattered lesions were also noted. In just over 50 per cent of patients a low sugar tolerance curve was obtained, this is suggestive of allergy. All the brown-eyed patients, 9 in number, had glycosuria. Whether there is an antigen responsible or whether it may be that worry or emotional stress brings about exhaustion of hormones and causes overwork of the endocrine glands, especially the adrenal gland, is not quite clear, but many of the symptoms suggest an endocrine basis.

957

Treatment

Use of thorium-X

Recent investigations into the treatment of lichen planus of the tongue have shown the curative effects of thorium-X, which can be applied directly in the form of a varnish to the affected area.

X-ray therapy

A single large dose of X-rays applied either to the spine or to the abdomen and chest has had good results (Hellier). About 29 per cent of the patients were cured and 41 per cent were improved. The effects of X-rays were produced by direct action on the skin and not because of changes in underlying nervous structures such as the spinal cord.

Hellier, F. F. (1943) *Brit J Derm*, 55, 11

Smith, Mary S. (1942) *Brit J Derm*, 54, 255

LIPOIDOSES

GAUCHER'S DISEASE

Diagnosis and differential diagnosis

Contributions by Chalmers and by Emanuel have indicated the value of sternal marrow puncture in the diagnosis of this disease. The full clinical picture includes (1) pain in the bones, often associated with radiologically recognizable areas of bone absorption due to deposition of the lipoid, (2) splenomegaly with or without hepatomegaly, (3) a haemorrhagic diathesis, (4) anaemia, (5) brownish-yellow conjunctival pingueculae, (6) grey-brown pigmentation of the legs. Emanuel notes that in one of his cases the pigmentation of the legs was due to haemosiderin deposition. Radiological examination of the bones is now the most helpful single point in suggesting the diagnosis. Especially characteristic are the translucent areas in the lower end of the femur with widening of the shaft of the bone, leading to a characteristic 'hock bottle' appearance, and erosion of the head of the femur. Since the lipoid involved is a nitrogen-containing cerebroside, blood lipoid nitrogen should be examined: the normal value is from 1.5 to 2.5 milligrams per cent. Bloem, Groen and Postma found the figure was raised to over 40 milligrams per cent in

964

- 964 3 out of 5 cases In one of Emanuel's cases the figure reached 29 milligrams per cent Characteristic large Gaucher cells, diameter 20-70 μ , with excentric nuclei and fibrillary or vacuolated cytoplasm may be found by careful search There is not any specific treatment Splenectomy and other operations are to be avoided when possible

Bloem, T F, Groen, J, and Postma, C (1936) *Quart J Med*, 5, 517

Chalmers, J N M (1940) *Arch Dis Childh*, 15, 230

Emanuel, E (1941) *Edinb med J*, 48, 843

LIVER DISEASES: I—LIVER FUNCTION TESTS

SCOPE AND SIGNIFICANCE

- 967 By the use of functional tests, chiefly the hippuric acid synthesis and the galactose tolerance test, a number of workers have demonstrated impairment of liver function in thyrotoxicosis (Haines, Magath and Power, Lichtman, MacLagan and Rundle, Althausen, Althausen, Lockhart and Soley) Haines, Magath and Power, however, do not find the hippuric acid test useful in assessing surgical risk, although MacLagan and Rundle, and Althausen find that the results with the galactose tolerance test are correlated to the basal metabolic rate and the clinical state of untreated patients That fatal thyrotoxicosis can cause microscopic liver damage has been shown by Wyndham, who found in 6 out of 43 cases an increase of portal connective tissue, lymphocytic infiltration, areas of regeneration and occasional minor foci of atrophy Investigations carried out among people over 60 years of age show that a considerable proportion of these persons yield evidence of dysfunction Many of the liver function tests have been disappointing The intravenous hippuric acid test (see below) is probably the most sensitive of the six well known modern tests in use Nevertheless in 52 cases of slight and moderate degrees of cirrhosis already diagnosed by modern methods, Mateer, Baltz, Marion, Hollands and Yagle found that only two-thirds of the results were positive

TESTS

Galactose tolerance test

King and Aitken describe a modified galactose tolerance test in which the blood galactose is determined at half-hour intervals after intravenous injection of 50 cubic centimetres of a 50 per cent galactose solution, in most cases it distinguishes clearly between obstructive jaundice, in which the blood galactose falls below 10 milligrams per 100 cubic centimetres at 2 hours, and toxic or infective (hepatic) jaundice in which it remains above that level Bassett, Althausen and Coltrin obtained similar results with a similar test, taking 20 milligrams per 100 cubic centimetres blood galactose at 75 minutes as the dividing line

Hippuric acid test

Interest continues in Quick's hippuric acid test (see Surveys and Abstracts 1940, p 386) DeLor and Reinhart find it a useful indication of prognosis, operative or otherwise, in cases of obstruction of the common bile-duct, although in a mixed group of diseases of the liver and gall-bladder disease (the latter predominating) the bromsulphalein test gave a larger number of abnormal results They emphasize the fact that in general normal liver function tests may not be taken to exclude hepatic disease Wilson found the hippuric acid test to be a more sensitive indication of liver damage than was the bromsulphalein test in a mixed group of non-surgical diseases involving the liver Cates, however, showed that only 18 out of 32 patients, in whom the presence of hepatic cirrhosis was proved by biopsy through a peritoneoscope, synthesized a subnormal amount of hippuric acid 22 out of 28 showed bromsulphalein retention

Mateer, Baltz, Marion, Hollands and Yagle compare the sensitivity and reliability of Quick's hippuric acid test, a modification of Macdonald's serial bromsulphalein test, Hanger's cephalin-cholesterol flocculation test and Gray's colloidal gold test with the two older tests, the oral hippuric acid test and the Rosenthal bromsulphalein test They recommend the cephalin-cholesterol flocculation test, Quick's test and the serial bromsulphalein test for routine use In non-jaundiced cases with suspected liver damage all three tests should be used, in jaundiced cases the flocculation test and Quick's test should be used, as the bromsulphalein test is not reliable when jaundice is present The colloidal gold test is too complicated for routine use The serial bromsulphalein test should take the place of the Rosenthal method

The serial bromsulphalein test

This is a modification of the original bromsulphalein test It is a very accurate one Persons to be tested are injected intravenously with 5 milligrams of the dye for every kilogram of their body weight Every 5 minutes thereafter during from a 10-minute to a 35-minute period the blood is examined colorimetrically and thus calculations can be made with regard to the rate of removal of the dye from the blood stream

Cephalin-cholesterol flocculation test

This test is based on the principle that serum from those who have had damage to

LIVER DISEASES

the hepatic tissues is capable of flocculating a colloidal cephalin-cholesterol suspension, this does not happen in a normal person

- Althausen, T L (1939) *Amer J digest Dis*, **6**, 544
— Lockhart, J C, and Soiley, M H (1940) *Amer J med Sci*, **199**, 342
Bassett, A M, Althausen, T L, and Coltrin, G (1940) *Proc Soc exp Biol*, N Y, **45**
Cates, H B (1941) *Arch intern Med*, **67**, 383
DeLor, C J, and Reinhart, H L (1940) *Amer J clin Path*, **10**, 617
Haines, S F, Magath, T B, and Power, Marschelle H (1942) *Ann intern Med*, **14**, 1225
King, E J, and Aitken, R S (1940) *Lancet*, **2**, 543
Lichtman, S S (1941) *Ann intern Med*, **14**, 1199
MacLagan, N F, and Rundle, F F (1940) *Quart J Med N S*, **9**, 215
Mateer, J G, Baltz, J I, Marion, D F, Hollands, R A, and Yagle, Elizabeth (1942) *Amer J digest Dis*, **9**, 13
Wilson, S J (1940) *J Lab clin Med*, **25**, 1139
Wyndham, N (1940) *Aust N Z J Surg*, **9**, 385

LIVER DISEASES. III—CHRONIC VENOUS ENGORGEMENT

PATHOLOGY AND MORBID ANATOMY

Day and Armstrong found, in the livers of 11 patients who died after long-standing chronic venous engorgement with raised systemic venous pressure, an increase of fibrous tissue of a highly characteristic type, which they consider due to the altered haemodynamic conditions and not to toxic or infective agents. Katzin, Waller and Blumgart, in a survey of 2,000 consecutive post-mortem reports, found fibrosis in 33 per cent of the 286 cases showing chronic venous congestion, compared with 12 per cent in the remainder. The extent of the fibrosis was correlated to the duration of the clinical signs of venous congestion, it was situated round the central vein (a site peculiar to the chronic venous congestion cases, in which it was not, however, due to condensation of reticulum) or round the portal tracts, or both. It seems, then, that long-standing venous engorgement of the liver does give rise to fibrosis. Only rarely, however, is it sufficiently advanced to influence the clinical picture, by producing the association of a small liver with raised venous pressure, ascites out of proportion to the oedema, and perhaps a palpable spleen.

- Day, T D, and Armstrong, T G (1940) *J Path Bact*, **50**, 221
Katzin, H M, Waller, J V, and Blumgart, H L (1939) *Arch intern Med*, **64**, 457

LIVER DISEASES. V.—HEPATITIS, ACUTE AND SUBACUTE CLINICAL AND AETIOLOGICAL TYPES

Arsphenamine jaundice

Incidence and causal factors

Concurrently with the world-wide increase in the incidence of infective hepatitis since 1939, there has been a striking rise in the number of patients in whom jaundice develops during arsphenamine treatment for syphilis. In a series of 1,965 soldiers treated for syphilis between 1940 and 1943, in 297—or 15 per cent—jaundice developed (Campbell). In 46 per cent the jaundice occurred during or immediately after the first course of treatment, in 37 per cent it occurred during the second course, and in the remainder during the third or fourth course. The clinical and pathological features of such cases admitted into the same wards at the Connaught Hospital, London, as were patients with infective hepatitis were indistinguishable from the afebrile form of the latter (Dixon), and McMichael found that the pathological appearance of the liver in biopsy specimens was identical. The facts that in less than 3 per cent of the patients with jaundice dermatitis also developed, and that none had albuminuria, show that arsenical poisoning is not the sole cause of the hepatitis. The recent rise in the incidence of jaundice in patients undergoing antisyphilitic treatment is probably due to the increased proneness to infective hepatitis which results from the toxic action of syphilis on the liver, and from treatment with arsenic which is also a liver poison. The vulnerability of the liver is perhaps further increased by some vitamin deficiency due to war-time lack of cheese, milk and butter, and in some cases by the toxic effect of alcohol. The prognosis is good, but it is unwise to give further arsenic injections however completely the patient may appear to have recovered from the hepatitis.

Jaundice due to other drugs and chemical poisons

Chloroform

Sheehan describes the pathological changes in 14 fatal cases of chloroform poisoning following the use of chloroform as an anaesthetic during labour. Necrosis in the middle zone of the liver lobules is the most constant change, and may be accom-

panied by central necrosis. The histories of these and other recorded cases strongly suggest that prolonged starvation before the administration of the chloroform is an important factor in rendering the liver susceptible to damage by it. Delayed chloroform poisoning occurred in patients who had been unduly long in labour and received little food, who had vomited copiously, or who had been therapeutically starved because they were eclamptic. This clinical observation receives support from the observations of Miller and Whipple and of Miller, Ross and Whipple. They found that a well-fed healthy dog tolerates from 60 to 90 minutes of light chloroform anaesthesia with little evidence of liver injury, whereas dogs whose protein stores have been depleted by low protein diets and removal of plasma die after 20 minutes of such anaesthesia. Their livers show necrotic changes. The protein-depleted dog can be protected against this fatal liver injury by a large meal of beef 36 hours before the anaesthetic, by the intravenous injection of plasma, and also most strikingly by the administration of the sulphur-containing amino-acid methionine. Cystine is effective, but to a lesser extent.

Sulphanilamide

Sulphanilamide and possibly the other chemotherapeutic agents related to it must be added to the list of drugs capable of producing 'hepatitis' and jaundice, although this is among the rarest of their untoward effects.

Other forms of acute and subacute hepatitis

Infective hepatitis

Aetiology—In normal times infective hepatitis is a disease of the winter months, mainly affecting children between the ages of 5 and 15 years. During the present war, however, infective hepatitis has been demonstrated in various regions and it was prevalent among European troops in North Africa, Malta, Syria and Palestine. During the past 15 years the incidence has increased not only in Great Britain but also abroad. That the British troops suffered at the rate of 11.5 per thousand from the disease whereas the Maltese troops had an incidence of 0.7 per thousand is ample proof of the susceptibility of Aryan peoples. Infective hepatitis has also been reported in the German army and in the occupied countries. All attempts to isolate a causative organism have failed and there is no evidence that the disease is spread by milk, water, food or vermin; direct contact by one person with another seems to be the chief method of spread. If a virus is responsible, its dissemination is brought about by droplet infection; another point in favour of virus infection is the fact that there is no leucocytosis. Alcohol lowers the response of the liver to infection of the virus of infective hepatitis (see *Pathology* below).

Clinical picture—In some cases jaundice is not seen and there are no changes in the stools and urine, the result of this is that there is difficulty in tracing the infection. The infective period lasts for about 7 days and the incubation period is approximately 28 days. The typical blood culture shows a monocytosis varying from 2 to 19 per cent. The symptoms are first headache, lasting for 2 or 3 days, with loss of appetite and slowing of the heart. Later on there is pain in the upper part of the abdomen with epigastric tenderness and enlargement of the liver. Vomiting may be severe, and finally jaundice appears with bile present in the urine. The patient is liable to have pancreatitis, and although in adults recovery is sometimes very slow the death rate is low.

Treatment—The treatment is most unsatisfactory and there is no specific remedy. So far as diet is concerned abundant carbohydrates and proteins with the minimum of fat should be the routine and an ample supply of fluid should be kept up. Physiological saline alternated with 10 per cent dextrose solution should be given intravenously by the drip method in cases in which vomiting occurs or when the patient is too drowsy to take sufficient fluid. One part of the treatment which may be stressed is that the patient should be kept in bed until the jaundice has disappeared completely and the liver and the spleen are not palpable. In any case the urine should be clear of bile. Dixon states that alcohol should be very carefully watched, the patient should be advised to remain teetotal for at least a year after he has recovered, thereafter he should be very moderate, invariably avoiding the taking of strong alcohol on an empty stomach.

Pathology—The nature of the lesion has been made free from doubt by the work of Dible, McMichael and Sherlock who by performing aspiration biopsy of the liver have proved that the condition is one of acute hepatitis, the lesions may be circumscribed or diffuse, or there may be patterns of these two types, if the jaundice lasts for more than 2 weeks, however, the zonal variety usually obtains. It should be noted with reference to the various lesions of epidemic hepatitis and those associated with arsphenamine and serum that the histological picture is the same in all cases.

Campbell, D. J. (1943) *Brit J Vener Dis*, 19, 63.

Dible, J. H., McMichael, J., and Sherlock, S. P. V. (1943) *Lancet*, 2, 402.

Dixon, H. B. F. (1944) *Encyclopaedia Medical Progress* (Critical Survey section), p. 35.

LIVER DISEASES—LUNG DISEASES

- McMichael, J (1943) Communication to Association of Physicians of Great Britain and Ireland
Miller, L L, Ross, J F, and Whipple, G H (1940) *Amer J med Sci*, 200, 739
— and Whipple, G H (1940) *Amer J med Sci*, 199, 204
Sheehan H L (1940) *J Obstet Gynaec*, 47 49

LIVER DISEASES. VI—HEPATITIS, CHRONIC

AETIOLOGY

Bloomfield has investigated the aetiology of chronic hepatitis in 41 patients with the clinical picture of the disease. In 36 there was a history of alcoholism, but in the others the aetiology was obscure. Particular inquiry was made for a previous attack of acute hepatitis, in 4 cases there was a history of jaundice, and Bloomfield thought that in some cases after complete clinical recovery from an acute attack of hepatitis a latent hepatic insufficiency might persist and progress, leading to chronic cirrhosis. The initial stages of chronic hepatitis might be entirely latent, or latent with periodical exacerbations.

974

The suggestion that a dietary deficiency is a factor in the causation of cirrhosis of the liver is given further support by the observations of Rich and Hamilton. They produced cirrhosis in rabbits, of a type resembling Laennec's cirrhosis in man, by feeding them on diets containing vitamins A, C, D and E but lacking yeast. The addition of yeast prevented the development of cirrhosis, but the effective ingredient was shown to be neither vitamins B₁, B₂, B₆, nor nicotinic acid, it may have been choline.

Gyorgy and Goldblatt have carried out further experiments on rats in order to determine the effects of diet on the liver, and they conclude that experimental dietary necrosis and cirrhosis is due to the dietary factors causing fatty infiltration, the administration of choline reduced the severity of the hepatic lesions, and the combined use of *l*-cystine and choline or of *dl* methionine was also highly effective in the prevention of hepatic disease.

- Bloomfield, A L (1938) *Amer J med Sci*, 195, 429
Gyorgy, P, and Goldblatt, H (1942) *J exp Med*, 75, 355
Rich, A R, and Hamilton, J D (1940) *Johns Hopk Hosp Bull*, 66, 185

LIVER DISEASES. VII.—INFANTILE HEPATIC CIRRHOSIS

NODULAR CIRRHOSIS OF THE LIVER AFTER ACUTE HEPATITIS

At the children's hospital of Goteborg, Sweden, in a period of 10 years 5 patients have been observed in whom nodular cirrhosis of the liver appeared after an attack of acute hepatitis. Ramhult gives a brief report on the first 4 and a detailed report on the fifth, a boy of 7 who had catarrhal jaundice in the autumn of 1935. The jaundice disappeared after 6 weeks but the patient continued to suffer from somewhat indistinct abdominal symptoms. He was admitted to hospital with melaena. He was anaemic, with haemoglobin 56 per cent. Examination showed slight bilirubinaemia, purpuric spots on the rectal mucosa, nodular enlargement of the liver, no ascites, no ectasia of oesophageal veins and no splenomegaly.

975

The first patient, a 14-year-old boy, had acute hepatitis in April 1926, and cirrhosis in August, he died in October. The second, a boy of 13, had hepatitis in December 1927 and cirrhosis in August 1928, he died in September 1929. The third, a girl of 8, had hepatitis in December 1931 and cirrhosis in January 1932, she died in November 1933. The fourth, a girl of 9, suffered from acute hepatitis in May 1932, cirrhosis was diagnosed in May 1933 and she died in November 1933. Necropsy was performed on all the patients who died and in each case confirmed the clinical diagnosis.

- Ramhult, A (1938) *Svenska Lakartidn*, 35, 871

LUNG DISEASES: I—ATELECTASIS AND COLLAPSE

Corrigendum

In Vol VIII, p 164, to the paragraph on acute massive collapse in the section on *Treatment*, a cross-reference should be added to LUNG DISEASES. POST-OPERATIVE COMPLICATIONS, p 236, where a section is devoted to the prevention and treatment of this condition.

AETIOLOGY

Among the aetiological factors of collapse, the relation between pulmonary collapse and infection of the accessory nasal sinuses has been pointed out by Paton Philip (personal communication), who demonstrated numerous cases of unilateral pulmonary collapse associated with infection of the maxillary antrum (sometimes with a fluid level) recognizable on X-ray examination. In many of his cases there was re-expansion of the affected lung, with return of the displaced heart and trachea to the middle line after the sinus infection had been surgically treated.

985

CLINICAL PICTURE

Lander has called attention to the significance of localized emphysema as evidence of localized pulmonary collapse. Davidson referred to this in a discussion at the Royal Society of Medicine in which the early diagnosis of intrathoracic new growths was discussed. According to Lander the diminution in size of a lobe due to obstructive collapse may cause localized compensatory emphysema recognizable in a skiagram and perhaps the only detail which indicates the presence of localized pulmonary collapse. In such cases the well known triangular shadow may be absent, and displacement of heart or mediastinum may not be evident. Something has to fill up the space created by the shrinkage of the collapsed portion of lung, and this is effected by the compensatory emphysema.

Davidson, M (1939) *Proc R Soc Med*, **32**, 1342

LUNG DISEASES: III.—ABSCESS AND GANGRENE

TREATMENT

Operative

- 987 Overholt and Rumel discuss the treatment of lung abscess based largely on the results obtained in treating 95 cases in the last 8 years, and contrast the high mortality rate (53 per cent) in the group of patients treated by various generally accepted therapeutic measures, *excluding external drainage and excision*, with the much lower mortality rate (23 per cent) in the group treated by lung resection. They criticize the traditional separation of lung abscesses into acute and chronic stages on a purely chronological basis without regard to the pathological condition present, as being unscientific and unsatisfactory.

Overholt, R. H., and Rumel, W. R. (1941) *New Engl J Med*, **224**, 441

LUNG DISEASES: IV.—TUBERCULOSIS

AETIOLOGY

Carriers

- 988 *Danger of the adult carrier*
Infection of children—Children suffering from pulmonary tuberculosis generally become infected because of contact with another human being, the younger the child the more serious is the condition, which arises from infection through the respiratory tract. Fleming showed in an analysis of about 350 fatal cases of tuberculosis in children that the usual end-lesion was tuberculous meningitis, nevertheless the primary focus was found in the lungs in from 74 to 80 per cent of cases. Since children under 4 years of age are especially susceptible these persons must be shielded from human infection by isolation of adult carriers. The young child with early infection does not require isolation but should live in good conditions in the country with an ample supply of milk, cod-liver oil and vitamin D.

CLINICAL PICTURE

Bronchogenic tuberculosis

Origin, diagnosis and management

The origin, diagnosis and management of early bronchogenic tuberculosis are discussed by Kayne, who considers that the term pulmonary tuberculosis requires elucidation. It is generally used to describe the disease seen in adolescents and adults, with slow progressive destruction of the lungs from intrabronchial invasion by bacilli and with cavitation. Other active lesions of the lungs, however, are common, namely the primary infection and the lesions caused by dissemination. The term, pulmonary tuberculosis, should include therefore any active lesion resulting from any phase of tuberculosis, the term, bronchogenic tuberculosis, should be limited to the common type of bronchogenic disease. Certain lesions caused by dissemination may resemble bronchogenic tuberculosis when cavitation appears, but contain little caseous substance and seldom cause intrabronchial transmission. The bronchogenic type begins as a single focus, generally in the upper lobe of the lung, which enlarges, liquefies and forms a cavity, and causes secondary foci from intrabronchial transmission. There may not be any physical signs or symptoms, but the condition can be detected by radiological examination. Bronchogenic tuberculosis must therefore be defined as the earliest recognizable caseous focus which can be detected radiologically, before it has penetrated a bronchus. This type of bronchogenic lesion occurs in patients who have already acquired resistance to a primary infection although this may be recent. The two common mechanisms causing the lesion are exacerbation of residual foci, and new exogenous re-infection with lowered resistance. Progressive chronic dissemination is an uncommon cause. The early lesion must be differentiated from other types, and occurs above or below the clavicle as a group of small foci, or as a homogeneous shadow. Serial radiographs assist the diagnosis. The mode of origin,

massive contact and resistance must be considered in the estimation of prognosis and treatment. Institutional treatment is usually essential. Rest in bed is indicated, with collapse therapy if regression is slow. The relation of bacilli in the sputum is discussed, and the importance of mass radiological examinations is stressed, with a critical examination of the method used.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Radiography

Mass radiography

The best contribution towards early diagnosis which has recently come forward is the introduction of mass radiography on miniature films. Diagnosis is not the only thing, doctors must be skilled in determining when the patient needs sanatorium treatment and when all that is necessary is a routine examination at regular intervals. It is now established as essential that in every case after clinical examination for pulmonary tuberculosis the patient should be sent to the nearest radiological centre for X-ray examination. According to Trail there are two aspects to be considered in mass radiography—the national and the individual. The outlook for patients treated by the best available methods depends upon the extent of the disease when it is diagnosed. The difficulty of diagnosis arises because of the fact that so few patients are aware of the dangers to them from the early lesion, there is no dramatic warning, and symptoms are often absent, if minor symptoms prevail they are disregarded. There is thus all the more reason for the provision of mass X-ray investigation. By this method it is possible to separate the acute cases from the chronic cases, the early case from the established case, above all it allows the tuberculous person who has not reached the stage of having physical signs to be examined and advised without delay to have intensive treatment.

Erythrocyte sedimentation test

Is its value overestimated?

Banyai and Cadden discuss the results of the erythrocyte sedimentation test as applied to 2,640 tuberculous patients at Mairdale Sanatorium, Wisconsin, for a period of four and a half years from 1939. Many theories have been advanced in explanation of the changes in the sedimentation in health and in disease, but there is not any doubt that the rate is subject to the Stokes physical law regarding the sinking of particles suspended in a fluid medium. The equation is $V = \frac{2}{9} g \frac{S - S_1}{u} r^2$,

when V is the velocity of the fall, g the gravitation constant, S the specific gravity of the erythrocytes, S_1 the specific gravity of the blood plasma, u the absolute viscosity of the plasma and r the radius of the erythrocyte aggregates. It will be noted that the right side of this equation contains 4 variables. Normally, erythrocytes settle faster in women than in men and the rate is increased by pregnancy, menstruation, exercise, hunger and old age, it may even be affected by the weather. It is therefore a test with many limitations and according to these observers compares unfavourably with serial radiographs of the chest. In 8 per cent of the 2,640 cases under review it was found to be normal.

Among routine tests, the blood sedimentation rate test must be used with great care. It must be remembered that there are various causes other than pulmonary tuberculosis for a raised sedimentation rate. As a guide to the prognosis of cases over a long period it is of value. A progressively lower rate is of better prognostic significance than one which remains high. The sedimentation test, however, should be used only in conjunction with all other findings, as otherwise it could in certain cases be misleading.

TREATMENT

Cure

Sanatorium treatment

The modern sanatorium should be self-contained if possible and the staff should be so trained and the equipment be such that all the latest forms of treatment can be carried out under one roof. Also, it cannot be too strongly stressed that a study of the psychological aspect of each patient is extremely important: a contented mind goes a long way towards helping to speed up the arrest of the disease.

It is essential that the patient after he leaves the sanatorium should be in the care of a doctor in whom he has faith, and that he should see the doctor at least once a month for the first 6 months. The patient should be examined by X-rays every 3 months for the first year and at 6-monthly intervals for the subsequent one or two years.

Gold treatment

The unsatisfactory conditions set up by gold compounds when the latter were administered intravenously led to the development of a therapy in which gold is combined in an oily preparation given by intramuscular injection. Oleosanocrysin is the preparation best known and is suitable on account of its slower absorption.

and of the fact that complications are reduced to the minimum. This type of treatment is contra-indicated when there is renal damage because gold is very irritant to renal tissues, although reactions quickly disappear when treatment is stopped. Apart from nephritis the most frequent complications to be expected are dermatitis, stomatitis and colitis. The doses are small, beginning with 0.05 gramme once a week and gradually increasing until the dose amounts to 0.20 gramme. When a total of from 5 to 7 grammes has been given there should be a latent period of 3 months in which treatment is stopped, then another course may be started. Statistics which have been published show that about one-fifth of the patients who are tolerant of gold compounds show undoubted improvement. The type of lesion which apparently reacts most successfully to oleosanocrysin is the exudative and infiltrating type which as a rule clears up very quickly. Rest considers that in pulmonary tuberculosis gold treatment should be looked upon as the last resort.

Chemotherapy

Sulphone derivatives

The most effective of the agents of the sulphone series is 4,4-diaminodiphenylsulphone (diaminosulphone). This substance inhibits the growth of the tubercle bacillus *in vitro* but it cannot be used *in vivo* because of its toxicity to man.

Artificial pneumothorax

Artificial pneumothorax remains one of the greatest advances in the treatment of the disease. It is being done more and more in the early type of case and now that it can be controlled by X-ray examination and screening before each refill, complications and dangers are becoming much less. Adhesions of the lung to the pleura are noticed, and divided as soon as possible. Cases of contra-selective collapse are noted within the first few weeks after the treatment has been commenced and if it is impossible to cauterize adhesions and make the collapse selective the pneumothorax can be abandoned before any undue complications occur.

Phrenic avulsion

Temporary paralysis of the phrenic nerve by crushing is most suitable for cases in which there are thin-walled apical cavities, the essentials are that if the cavity should be closed in this fashion, the patient should be examined by X-rays every week and that immediately the diaphragm shows evidences of greater movement, the nerve should be crushed once more and maintained in its crushed position until there is no danger that the cavity will reopen.

Extrapleural pneumothorax

Extrapleural pneumothorax still has a place in the treatment of pulmonary tuberculosis but it must be confined to recent cavities in the upper lobe of the lung, which are not surrounded by dense thickened pleura. A great deal of the success of the extrapleural operation depends upon its after-care, it is essential to make an X-ray examination of the patient daily, to remove any fluid that forms and to refill daily for at least 10 days, and then every other day for a further fortnight, after which the intervals can be extended to a week. Most extrapleural conditions do best if refills are given weekly during the whole of the time that the patient is having this form of treatment.

Thoracoplasty

The technique of thoracoplasty continues to improve and since local anaesthesia has been adopted in this operation the after-effects are not so severe. Of late years the type of case subjected to this operation has changed considerably. Whereas for some time it was stated that only those patients with unilateral disease in which fibrosis was taking place should be operated upon, the operation is now quite often performed in cases of bilateral disease in which the disease on one side is extensive and active and on the other side fairly limited in extent. By doing a thoracoplasty on the worse side the surgeon gives the other lung a better chance of healing owing to the eradication of toxæmia.

Total pneumonectomy

Total pneumonectomy is now being employed in pulmonary tuberculosis. The mortality is about 40 per cent. In the opinion of most authorities the operation should always be preceded by thoracoplasty with extrafascial apicectomy. Pneumonectomy should be done when there is bronchial occlusion or a condition of stenosis which cannot be treated by bronchoscopic dilatation. If a branch bronchus is affected lobectomy should be satisfactory, and here the mortality is from 5 to 20 per cent.

The Monaldi drainage tube

The use of the Monaldi drainage tube in the treatment of large apical cavities which have been called 'tension cavities' has come to the fore. In most cases it is of benefit in diminishing the size of the cavity prior to thoracoplasty but as a treatment *per se* it has not given a great number of satisfactory results. It is important in using this treatment to choose the case carefully. Repeated X-ray examinations must be carried out during the treatment in order to watch the effect on the size of the cavity.

- Banyai, A. L., and Cadden, A. V. (1943) *Arch intern Med*, **72**, 245
 Fleming, G. B. (1943) *Lancet*, **2**, 580
 Kayne, G. G. (1941) *Brit med J*, **2**, 154
 Rest, A. (1943) *Amer Rev Tuberc*, **47**, 406
 Trail, R. R. (1943) *J R Inst publ Hlth Hyg*, **6**, 311

LUNG DISEASES. VII.—FIBROSIS

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Hebert states that, when an incorrect diagnosis of fibrosis is made as a result of radiological examination, this is generally due to the fact that a wrong interpretation has been placed on positive shadows cast by inflammatory changes. He considers that fibrosis is diagnosed much too freely in cases of tuberculosis, that a general fibrosis is not infrequently diagnosed in cases of chronic pulmonary catarrh on the evidence of increase in the density or thickness of the pulmonary markings or from the appearance well described as increased arborization, and that there is often a failure to diagnose chronic interstitial pneumonia when, and because, positive shadows are lacking. The author made the following generalizations concerning the radiological diagnosis of fibrosis: (1) Contraction of the lung, or of part of it, as evidenced by displacement of the heart or trachea, by change in the conformation of the ribs or the height of the diaphragm, or by crowding together of pulmonary markings, is good evidence of fibrosis if collapse, lobar or lobular, can be excluded. (2) Neither a generalized nor a localized interstitial fibrosis should be diagnosed on the evidence of linear shadows unless the latter are well marked or conform to a type met with in some forms of silicosis. (3) Multiple nodular markings should be regarded as due to an inflammatory process, unless they are sharply defined or of a type found in silicosis. (4) A generalized peribronchial fibrosis, such as may accompany chronic bronchitis, can rarely be distinguished with certainty from a chronic inflammatory process without fibrosis, but the presence of general emphysema is suggestive inferential evidence. (5) Neither the density nor the thickness of the wall of a round cavity can, in itself, be regarded as evidence of fibrosis. (6) Coarse linear bands, especially if in the neighbourhood of an interlobular fissure, as well as certain elongated shadows, are more often due to an exudative process than to fibrosis.

Hebert, G. T. (1939) *Tubercle*, **20**, 145

LUNG DISEASES. VIII.—TUMOURS

MALIGNANT TUMOURS OF LUNGS AND BRONCHI

Primary

Diagnosis

The method, introduced by Dudgeon and Wrigley, of examining fresh films of sputum for the presence of malignant cells is being increasingly used, and in a number of cases enables a diagnosis of malignant disease of the respiratory tract to be made when all other investigations have been indefinite. The method is as follows:

A fresh specimen of sputum is poured on to an unglazed porcelain tile. Film preparations, preferably of blood-streaked or solid portions, are made by spreading with a scalpel on a glass slide. The wet films are fixed in Schaudinn's fluid (one volume of absolute alcohol and 2 volumes of a saturated aqueous solution of mercuric chloride—to which is added immediately before use glacial acetic acid to a strength of 3 per cent), the slide is immersed in the fixative for 20 minutes if possible, but 2 minutes will suffice. It is transferred to methylated spirit containing a few drops of solution of iodine and washed in distilled water. The film is stained in Mayer's haemalum for 2 minutes or less, and blued in tap water. Over-staining must be avoided. It is counterstained in eosin, dehydrated through the usual series of alcohols, cleared in xylol, and mounted in Canada balsam with a coverslip. About 6 films should be made from each specimen of sputum.

The results of sputum examination in 58 cases of suspected malignant disease of the respiratory tract are recorded. More recently Barrett has reported favourably on this method. Malignant cells have also been demonstrated in centrifuged pleural fluid.

NON-MALIGNANT INTRATHORACIC TUMOURS

Morbid anatomy

Cystic disease of lungs

Excluding dermoid and parasitic cysts and saccular bronchiectasis, Wood classifies the forms of cystic disease of the lungs as follows: (1) Balloon cysts, occupying a large part of the lung, usually in infants or young children, may, by causing attacks of acute dyspnoea, imitate a pressure pneumothorax. The X-ray picture by showing the presence of pulmonary markings at the extreme apex or base and the absence of collapsed lung at the hilum is valuable in the diagnosis from pneumothorax. (2) Solitary cysts, smaller than balloon cysts, may imitate an emphysematous bulla or a tuberculous cavity. (3) Multiple cysts. (a) bubble cysts, the grossest form of cystic disease, by which the whole lung is often transformed into medium-sized

cavities, radiologically resembling air-containing intestine in a diaphragmatic hernia, (b) berry cysts of a smaller size forming grape-like clusters, often in the upper lobe, thus fibroid tuberculosis is suggested, the occurrence of haemoptysis favouring this diagnosis. These cysts are outlined by iodized oil. Found in foetal life and at all ages, the cysts contain air, are connected with the bronchi, and their walls resemble the bronchial wall. They appear to be due to a failure in the extremely complicated development of the lung budding, which stopped prematurely and swelled out. Microscopically the walls of the cysts show disordered growth, not degeneration. Cystic disease of other organs may be present. Patients with cystic disease of the lungs are in constant danger of secondary infection, which may be very severe.

Clinical picture

Bronchial adenoma

Foster-Carter publishes an extensive review of bronchial adenoma and describes 22 cases seen at Brompton Hospital, London. 62 per cent of the cases occurred in females, and the average age of onset was 28 years. Complete removal is difficult and recurrences are common. The tumour has been considered to be potentially malignant, but metastases have not been recorded. The growth probably develops from mucous glands and has been regarded as being identical with the benign unmixed salivary gland tumour. Thirty-three per cent of cases show a typical highly differentiated glandular structure, and the others are more or less undifferentiated, but both types run a long course, the average being 2 years in survivors. Treatment, which should be given early, consists in the prevention of symptoms—(1) directly due to the adenoma, namely cough and haemoptysis, and (2) due to obstruction and collapse—by simple bronchoscopic removal with local irradiation. The latter include the so-called asthmatoïd attacks, with paroxysmal dyspnoea, recurrence, indicating extrabronchial extension, requires intrabronchial manipulation, or removal of the lung tissue involved, or lobectomy if secondary infection and suppuration have supervened.

Treatment

Primary tumours

Total pneumonectomy—The important results reported by Ochsner and DeBakey with regard to total pneumonectomy prove that this method of treatment is the only hope of satisfactory cure in primary carcinoma of the bronchus. A recovery rate of over 40 per cent was recorded, but on the other hand nearly all of the remaining patients soon died. At present it is not possible to say on what the prognostic elements are based, each case must be judged on its own merits. Yet, on the whole, 10 years of trial have amply proved that pneumonectomy is in effect essential if any hope of recovery is to be entertained.

Irradiation—If pneumonectomy is impossible, irradiation and deep X-ray therapy may be considered, although statistics regarding the former do not give much hope. Treatment by radon (Ormerod) may prolong life for about 6 months at the most, and symptoms are emphatically relieved. Controversy still goes on regarding the value of deep X-ray therapy, however.

Barrett, N. R. (1938) *J. thorac. Surg.*, 8, 169

Dudgeon, L. S., and Wrigley, C. H. (1935) *J. Laryng.*, 50, 752

Foster-Carter, A. F. (1941) *Quart. J. Med. N.S.*, 10, 139

Ochsner, A., and DeBakey, M. (1941) *Arch. Surg., Chicago*, 42, 209

Ormerod, F. C. (1941) *J. Laryng.*, 56, 1

Wood, W. B. (1940) *Proc. R. Soc. Med.*, 33, 335

LUPUS ERYTHEMATOSUS

CLINICAL TYPES

Acute fulminating type

Clinical picture

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There are certain outstanding features of the acute fulminating type of lupus erythematosus. (1) The patient is profoundly toxic, and usually is torpid and apathetic or sunk in a toxic stupor. (2) The disease attacks many organs besides the skin. The mucosae are affected as is shown by the silvery flecking of the borders of the lips, erosions of the buccal mucosa and glossitis, in some cases haematemesis and colitis indicate that the gastric and intestinal mucosae are involved. The subcutaneous lymphatic glands and the spleen are enlarged. Purpuric lesions, petechiae and retinitis show that widespread changes are occurring in the smaller blood vessels, leucopenia and profound aplastic anaemia indicate that the haemopoietic system is assailed. (3) Two features are fairly constant but their significance is unassessed: the first is amenorrhoea, the second is alopecia, which may be patchy or diffuse, but is usually severe. (4) The characteristics of the eruption need not be emphasized here, except

to mention that Coburn and Moore have recently described pathognomonic changes in the hands, these changes consist in the appearance of purpuric lesions of the finger-tips which extend under the nails, the finger-tips being swollen but not tender, these authors have also described atrophy and necrosis of the dermis occurring round the margins of the finger-nails, and the appearance of haemorrhagic plaques on the palms (5) Atypical verrucous endocarditis, although not an outstanding feature, is noted in a proportion of cases which reach necropsy The condition is sometimes referred to as Libman-Sacks endocarditis Contratto and Levine have reported on a case in which cardiac signs were elicited, namely delay in the auriculo-ventricular conduction, in the early course of the disease before the cutaneous lesions of disseminated lupus erythematosus appeared (6) Usually death is due to pneumonic processes and renal failure

Disseminated fulminating type

Biochemistry

Vitamin C (ascorbic acid) is either destroyed or retained in the tissues, for the blood vitamin C levels are low and cannot be raised by adequate intravenous administration of the acid Blood calcium levels are low Blood pantothenic acid is increased Coburn and Moore have consistently found hyper-gamma-globulinaemia and as a result of this abnormality the erythrocyte sedimentation rate is increased and fluctuating false positive Wassermann reactions may be noted There is inversion of the albumin-globulin ratio in the serum although the total protein is usually within the normal range

TREATMENT

General

Barber finds that treatment with sulphonamide drugs benefits the eruption when it appears to be due to streptococcal infection but does not affect that which appears to have a tuberculous origin He considers that the reactions which may ensue after the giving of sulphonamide drugs are not simple reactions to the drug but are due to the liberation of streptococcal toxin by the action of the drug on latent foci of infection

MacKenna's experience in 1939 and 1940 has confirmed the value of sulphapyridine therapy in the treatment of many cases of the disease Small doses are desirable for most patients His experience has confirmed Chajes's statement that germamin (suramin, Bayer 205) is of benefit in some cases of the chronic discoid type

Weiner concludes that in cases of disseminated lupus erythematosus, sulphanilamide administered early in the disease in large doses (for example, from 7 to 12 grammes daily) is a practical measure which may be successful, provided that the skin is protected from sunlight and that all the precautions required in sulphanilamide treatment are taken

Chronic discoid type

Important factors in treatment

(1) The patient should be warned against exposure to bright sunlight or cold, for both will aggravate the disease, the former being the most dangerous The prescription of a sun-screening type of application to be applied to the lesion-bearing area is advocated by Stokes, who recommends for this purpose a cream or lotion containing 15-30 per cent of titanium dioxide, to which 5 per cent of disodium naphthol-sulphonate may be added (2) Drugs should not be prescribed or administered until the patient has been submitted to a stringent investigation It is useless to insert deposits of bismuth in the gluteal muscles when elsewhere there is a gross focus of streptococcal infection which can be eradicated by surgical means only (3) It should be remembered that injudicious therapy, particularly by means of gold salts, may cause an exacerbation of a latent focus of tuberculous infection, or may convert a simple discoid eruption into a generalized lupus erythematosus It should also be remembered that therapy with heavy metals may have a deleterious effect on the kidneys Therefore during therapy the cases should be assessed not only by the appearance of the patients' skin but also by routine investigation of their general condition (4) If there is reasonable evidence that the disease is streptococcal in origin, sulphonamides may be useful There is not any agreed scheme of dosage Glyn-Hughes and Spence claim good results by the administration of a course of approximately 25 grammes of sulphapyridine given over a period of 4 weeks Smith advocates giving 6 grammes of sulphanilamide a day for 4 days, followed by 3 grammes a day for a further 4 or 5 days if the drug is tolerated He states that usually 2 or 3 courses of sulphanilamide are required Other authorities are much more conservative in their dosage Barber has described various reactions to sulphonamides occurring in patients with lupus erythematosus It must be remembered that sulphonamides are double-edged weapons, and in their use the usual precautions,

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such as those given in the Medical Research Council *War Memorandum No 10*, must be observed (5) Good results have been claimed for therapy by means of intramuscular injections of bismuth or intravenous injections of gold preparations (6) The administration of autogenous vaccines made from cultures taken from the stools or from foci of infection is beneficial in a few cases (7) Localized lesions, especially of the indolent type, may be satisfactorily treated by applications of solid carbon dioxide

Barber, H W (1940) *Lancet*, 1, 583

Chajes, B (1938) *Lancet*, 2, 1288

Coburn, A F, and Moore, D H (1943) *Johns Hopk Hosp Bull*, 73, 196

Contratto, A W, and Levine, S A (1939) *New Engl J Med*, 221, 602

Glyn-Hughes, F, and Spence, A M (1940) *Brit med J*, 2, 741

Medical Research Council (1943) *War Memorandum No 10* London

Smith, A G (1943) *Med Pr*, 210, 246

Stokes, J H, and Associates (1942) *Fundamentals of Medical Dermatology*, 7th Revision Philadelphia

Weiner, A L (1940) *Arch Derm Syph*, N Y, 41, 534

LYMPHATIC GLANDS DISEASES

CHRONIC AFFECTIONS

New growths

Secondary

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Desjardins states that from the point of view of malignant metastases the retroperitoneal lymphatic glands, although perhaps not so often affected as the cervical glands, are the most important in the body. But, owing to their relative inaccessibility, little attention has been given to the relation between their involvement and the clinical picture produced.

Anatomically the abdominal and pelvic lymphatic glands form a continuous system, but for purposes of description they may be divided into two main groups (1) the iliac glands, and (2) the abdomino-aortic glands which are subdivided into (a) the mesenteric, and (b) the para-aortic or juxta-aortic. Practically all the lymph from the abdominal and pelvic organs, as well as from the lower extremities, must pass through the para-aortic glands or through both the mesenteric and the para-aortic glands.

Many patients with carcinoma of the bladder, prostate, uterus or rectum, or who have previously undergone partial or complete surgical removal of these organs, seek medical advice because for some time they have experienced fresh symptoms—backache, abdominal pain, flatulence, and belching after meals, increasing size of the abdomen and constipation. In addition to these symptoms of retroperitoneal metastases there may be increased deep resistance and tenderness on abdominal palpation in the epigastrium and in the umbilical, and sometimes in the hypochondriac, regions. Lymph from the testes and ovaries normally drains directly into the upper para-aortic gland, and malignant tumours of the testis never give rise to secondary growths in the inguinal glands until the growth in the testis has perforated the capsule of the organ, the same is true of some primary tumours of the ovary. The same symptoms are caused by retroperitoneal metastases as are those described in connexion with the bladder, prostate and rectum. The clinical picture of retroperitoneal glandular involvement by Hodgkin's disease and lymphosarcoma differs somewhat from those given above (see under Hodgkin's disease, p 128).

Chronic affections of undetermined origin

Giant follicular lymphadenopathy

Comparison with Hodgkin's disease—The comparatively newly discovered disease known as giant follicular lymphadenopathy is the subject of a paper by Symmers who states that clinically it is nearly always mistaken for Hodgkin's disease. Both are characterized by general or sometimes localized enlargement of the lymph glands and often by splenomegaly. Histologically they differ greatly from one another. In Hodgkin's disease the histological picture is complex. Initial hyperplasia of the lymph follicles is soon succeeded by diffuse lymphocytic, monocytic and giant-cell infiltration, eosinophil cells may be present. Later connective tissue overgrowth takes place, with the formation of dense hyalinized bands or patches which may so obscure the earlier changes as to render diagnosis difficult. In giant follicular adenopathy the histological changes are simple, consisting in great increase in number and size of the lymph follicles. In some cases the cells are of mature type, in others they are embryonic in appearance, with very large nuclei which stain feebly or not at all and sharply defined, often indented nuclear membranes (shadow cells), or of transitional type. The disease is usually benign, and spontaneous shrinkage or disappear-

ance of the glands may occur, although recurrence is not uncommon. This type responds promptly to mild X-ray therapy. Interference with venous return and serous effusions may occur. In some cases malignant changes develop, the cells spread from the follicles throughout the gland and polymorphous-cell sarcoma supervenes. In other instances the disease undergoes transformation into a variety of leukaemia. In the three necropsies so far reported foci of the disease have been found in practically all organs in which lymphoid tissue deposits normally exist. It appears that giant follicular adenopathy affects primarily the deeper lymphatic glands and that the enlarged superficial glands are secondary. A form, apparently primary, in the spleen has been described. The cause of the disease is unknown.

Desjardins, A. U. (1939) *Arch Surg, Chicago*, **38**, 714

Symmers, D. (1942) *Arch Path*, **34**, 385

LYMPHOPATHIA VENEREUM

CLINICAL PICTURE

MacNie reports on observations on patients with uveitis and kerato-conjunctivitis, and concludes that the virus of lymphogranuloma venereum is one of the causes of the oculo-glandular syndrome of Parinaud, and may be a cause of other ocular inflammations, particularly of the uveal tract.

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DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Rake, Shaffer, Grace, McKee and Jones state that lygranum antigen, prepared from the yolk-sacs of chicken embryos infected with the causative virus, appears to provide a satisfactory reagent for use in the Frei intradermal test, and is superior to the mouse-brain antigen in sensitivity and specificity.

TREATMENT

Tejeda comments on the treatment by xylol of 10 patients with positive Frei reactions, this was given in milk, starting with 50 drops daily, increased to 100 drops daily in divided doses. The pain ceased after the third day of treatment, the swelling disappeared, and ulcers healed within 25 days.

MacNie, J. P. (1941) *Arch Ophthal, N.Y.* **25**, 255

Rake, G., Shaffer, M. F., Grace, A. W., McKee, Clara M., and

Jones, Helen P. (1941) *Amer J Syph*, **25**, 687

Tejeda, L. H. (1941) *Bol Ofic sanit pan-amer*, **20**, 1005

MALARIA

AETIOLOGY

Incidence

Altitude

Of topographical conditions influencing the incidence of malaria the most important is perhaps altitude. In northern latitudes even very moderate altitude suffices to ensure freedom from malaria, largely because malarious areas are for the most part swamps and marshy ground in which the carrier chiefly finds its most suitable conditions. In the subtropics and tropics altitudes of some thousands of feet are very generally necessary to produce any pronounced effect, and mountainous country of moderate elevation may be highly malarious when the important carriers are of species which breed in streams. The effect of altitude is mainly due, it is believed, to reduced facilities for breeding of the carrier species, but temperature may also play a part.

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Transmission of malaria by blood transfusion

Preservation of blood at low temperatures does not destroy the malarial parasites, the danger may be much lessened if blood donors suffering from malaria or suspected to have malaria are given 10 grains of quinine once a week.

So far as liquid plasma is concerned, if it is preserved for 2 weeks in a liquid state it is harmless. Dried plasma is also safe.

Infection from syringes and similar instruments

Heroin drug addicts make common use of hypodermic syringes and therefore as most reported in New York City, for instance, where malignant tertian malaria is endemic, malaria occurred almost exclusively among such addicts, the infection being direct.

Malaria may be conveyed also through the syringe or other device used in giving successive intravenous injections of drugs such as neoarsphenamine. This is due to the blood being drawn back from the vein when ensuring due entry of the needle, infected corpuscles then clinging about the glass and being injected at a subsequent operation. Chung, Chu and Wang describe 22 cases of the disease in which the infection was traced to narcotic dens in Peiping.

Life cycle

In the host

Difficulty in finding parasites—During the first few days in primary malaria attacks it may be impossible to find parasites. This is especially so with *Plasmodium vivax* but less so with *P. falciparum* infections (Shute and Badenski).

Development of the sporozoite immediately after inoculation—It is still too early to say what processes are involved in the development of the sporozoite immediately after inoculation. It appears probable, however, that the sporozoites, at least in the bird parasites, become exo-erythrocytic forms capable of producing either further exo-erythrocytic cycles or endo-erythrocytic forms which can only produce their own kind. The type of cells in which *P. gallinaceum* sporozoites develop into exo-erythrocytic forms has been shown by Schulemann and Spies to be the histiocytes. The presence of bodies considered to be pigmentless parasites of this nature has been recorded also in the bone marrow in human cases of malaria, for example Raffaele records such in one case of *P. falciparum* and 2 cases of *P. malariae* infection. The exo-erythrocytic forms appear to be highly resistant to all kinds of drug treatment.

Blood examination

Methods of staining blood films

Various methods of staining films have been put forward, generally with the intention of shortening the time required in manipulation. Whittingham states that a saturated solution of Leishman stain in methyl alcohol (not methylated spirit as reported) keeps in an air-tight pot for many months although used daily for staining slides. Unfixed films are left in the pot for 5 minutes, washed quickly in distilled water and then dried. Field¹ has described a method for staining thick films so that the haemoglobin serves to bring out contrast. Films are stained unfixed in two solutions much as in the original watery Romanowsky method. Solution A consists of 0.16 per cent medicinal methylene blue and 0.1 per cent azure 1 (both obtainable from Gurr, London) and solution B of 0.2 per cent eosin (yellow, water-soluble, from British Drug Houses). Both solutions are made up by dissolving the stains in isotonic phosphate buffer, that is disodium hydrogen phosphate 5.0 grammes, potassium dihydrogen phosphate 6.25 grammes, water 500 cubic centimetres. Slides are placed for 1 second in A, rinsed for a few seconds in running water until no more stain comes away, and then for 1 second in B, followed by rinsing and rapid drying in a vertical position. The best staining is given at the bottom of the film. The same author² also describes very fully the different appearances shown by parasites of the different species in thick films. Boye also uses, as very suitable for camp work, a double watery Romanowsky for staining dehaemoglobinized and fixed thick films. These are placed for 15–20 seconds in 1:1,000 eosin, washed with a fine stream until no further stain comes away, and then for 40–45 seconds in Stevenel's blue. Stevenel's blue is methylene blue 1 gramme dissolved in 75 cubic centimetres of water and medicinal potassium permanganate 1.5 grammes in a separate 75 cubic centimetres. The solutions are mixed and placed for at least half an hour in the water-bath. A heavy precipitate is formed on mixing which dissolves and becomes deep violet on heating. It is ready for use after filtering. Although these and other methods are from time to time recommended for thick films it is doubtful if anything simpler can be employed than the pipetting of Giemsa diluted 1 drop to 1 cubic centimetre on unfixed slides placed on a sheet of glass as described in the *Encyclopaedia*, Vol. VIII, p. 314, the important point being that the films should not be too thick.

Rapid staining technique

Field¹ has described a simple and rapid method of staining malarial parasites in thick blood smears. The stain consists of brilliant cresyl blue 1 gramme, disodium hydrogen phosphate (anhydrous) 1 gramme, potassium dihydrogen phosphate 1.25 gramme, and distilled water to 100 cubic centimetres. The blood smears should not be more than 50 μ thick. The smears are rapidly dried by waving in air or a hot-air current, and lightly heat-fixed by passing through a flame for about a second. To stain the smears, the slides are dipped for 1 second into a jar containing the stain, immediately removed, and rinsed for 5 seconds by being drawn gently backwards and forwards in a vessel of clean tap water. When dry they are ready for microscopical examination.

Nomenclature and description of parasites

Distinct species in the chimpanzee

Brumpt has demonstrated that the parasites of the chimpanzee which closely resemble the three common human parasites readily give rise to infection when inoculated into the chimpanzee, but not in man. They must therefore be considered as related but distinct species. The *P. falciparum*-like parasite had already been

named *Plasmodium reichenowi* and the author has given the names *P. schweizeri* and *P. rodhami* to the *P. vivax*-like and *P. malariae*-like forms respectively

THE CARRIER

Behaviour in relation to transmission

Anopheles gambiae in Brazil

A. gambiae according to Pinto was introduced into the state of Rio Grande del Norte between August 1928 and February 1930, the ultra-rapid steamships doing the journey from Dakar (West Africa) to Natal (Brazil) in less than three days. In 1931 there was a great malaria epidemic in the districts near the harbour of Natal. In 1938 malaria was pandemic in Rio Grande del Norte and Ceara. *A. gambiae* is now reported from 45 localities in this latter state. This is the only case known of an anopheles extending its area of distribution in this remarkable manner.

Behaviour of *Anopheles minimus*

Important results have followed on the intensive study in the field of the behaviour of *A. minimus*, one of the most important carriers of the Far East. This species nearly always breeds in watercourses with grassy edges and it has been found that it may be eliminated by shading the breeding-places heavily with vegetation. Thomson, investigating this species in Assam, found that shade itself is highly attractive to the ovipositing female. Shading is effective only if dense enough to produce as a secondary effect the elimination of fringing vegetation. This increases the rate of flow at the edge, and since the female avoids water flowing even at the rate of 1 foot in 20 seconds, this tends to prevent oviposition. Larvae also tend to be swept away. The same effect is produced by exposure to light and by freeing the edges of vegetation. The temperature in shallow stagnant rice-fields may reach 41° C which is lethal to *A. minimus*, but not to *A. hyrcanus*, *A. barbirostris*, or *A. vagus* normally found in such a situation. The thermal death point of the last-mentioned species was found to be as high as 45° C. The temperature of running water was rarely found to be above 35° C.

PATHOLOGY AND MORBID ANATOMY

Changes in the organs

Microscopical appearances

Changes in bone marrow—According to Bianchi post-malarial anaemia, as shown by a study of the bone marrow obtained by sternal puncture in the human subject, is due to the changes brought about in this tissue. The fundamental condition is hyperplasia of erythroblastic cells with abnormal cell development and the presence of atypical forms of cells (megaloblasts with misshapen nuclei and of abnormal size). This is associated with hypoplasia of the haematoblasts, and also with hyperplasia of the cells of the reticulo-endothelial system, hypoplasia of the granulocytes and abundance of plasma cells and lymphocytes.

Macrophages—The conditions relative to immunity in malaria have been very clearly summarized by Sinton^{1, 2}. Briefly, in the first stage, corresponding to natural immunity, the macrophages attack sluggishly and non-specifically. Such action is relatively ineffective. A later stage follows in which not only are the numbers of macrophages greatly increased, but individual macrophages are much more active and such activity is specific, due to humoral changes giving rise to specific substances probably of the nature of opsonins. In this second stage, corresponding to acquired immunity, the phagocytosis of parasites is intense and very effective. The two conditions of increase in the number of macrophages (proliferation of the macrophage system in the liver and spleen) and specific humoral opsonic effect are not necessarily coincident, for example in a heterologous infection the macrophage system may be developed from the previous initial infection, but the correct humoral opsonins will not at the onset of the second infection be in existence to deal with this. There is thus sluggish macrophage action even although the macrophage system is hypertrophied. The circumstances have been likened to an increase in the numbers of a police force which, however, is ineffective without the suitable legal powers to arrest criminals. Suitable legal powers without a sufficient force would be equally ineffective.

All parasites do not necessarily behave in quite the same way in all details. Sinton, Hutton and Shute^{1, 2} found that *P. ovale* gives rise to more marked and more lasting resistance than does either *P. vivax* or *P. falciparum*. This may be the explanation why there are few or no relapses in this infection and why this parasite is usually confined to young children in the areas where it occurs, adults being made permanently immune.

Serological and other changes

Henry's reaction

Researches into the nature of the flocculation reactions known as Henry's reaction continue. The diagnostic validity of these tests appears to be established. Trensztar has summarized the position. During an attack the determination is of little importance compared with the search for parasites. But, in a patient who has recently been

febrile and whose blood does not show parasites, negative results with Henry's reaction are of value as excluding malaria as a cause of that fever

Melano-flocculation

Chorine, believing that melano-flocculation is entirely a matter of precipitation (flocculation) of the euglobulins, points out that the greater the proportion of insoluble protein the more rapidly will the instability leading to flocculation be brought about, either by addition of distilled water or addition of acid or, more critically, by lowering the pH towards the iso-electric point of the globulin. Malarial euglobulins have no special affinity for melanin, the inclusion of which in the precipitate merely acts as a more delicate indicator. Wolff, developing Chorine's technique, employs the following procedure. Tubes are prepared each holding 1 cubic centimetre of diluted buffer mixtures prepared from Baird and Tatlock's Universal Buffer Mixture varying from pH 8.4 to 5.00 in graduated steps of 0.04. To each tube in the series is then added 2 drops of the serum to be examined. The tubes are shaken and left standing for 5 minutes before readings are taken. The conditions are recorded as opalescent, faint cloudiness, cloudiness and marked cloudiness. Normal serums rarely show more than faint cloudiness at pH 7.0 and only an opalescence at 7.4. Strongly positive serums on the other hand show cloudiness or marked cloudiness up to 8.0 or 8.4 or beyond. Weakly positive serums show cloudiness from 7.4. For practical purposes two tubes (7.0 and 7.4) are sufficient. For preparing the serum 3 cubic centimetres of venous blood is placed in a dry centrifuge tube and, after the clot has formed and loosened, the tube placed overnight in a refrigerator. If the serum is not clear it is centrifuged. The results from 350 serums were closely comparable with those shown by the melano-flocculation test.

Congo red-quinine hydrochloride flocculation

Asai found that the flocculation of congo red by quinine hydrochloride was increased by the presence of globulin and was diminished by the presence of albumin. A test carried out on this basis was positive in malaria in 19 out of 21 acute cases, in 19 out of 21 latent cases and in 49 out of 54 chronic cases. It was positive also in kala-azar, liver diseases, syphilis, typhoid fever and pneumonia.

Complement fixation

Although positive results with complement fixation have been recorded by a number of earlier workers, so far a practical or certain outcome has not resulted from this method of diagnosis. The use of massive isolation of parasite substance obtained from heavily infected rhesus monkeys with *Plasmodium knowlesi* has, however, led to renewed experiment. Dulaney and Stratman-Thomas, Stratman-Thomas and Dulaney, and Dulaney, Stratman-Thomas and Warr have, by using such parasite substance as antigen, obtained strong reactions in human malaria. The deposit of parasites obtained by centrifuging the blood of parasitized monkeys is washed free of haemoglobin, dried *in vacuo* and ground to powder. For use 0.1 gramme of powder is ground in a mortar with 10 cubic centimetres of saline. The suspension thus formed is frozen and thawed four times with dry ice-alcohol mixture, it is then centrifuged and the supernatant fluid is standardized against known positive and negative malaria serums and tested for anti-complementary action. Of 117 patients with blood positive smears (76 *P. vivax* and 14 *P. knowlesi*) 90 gave a positive result, whereas of 194 patients with blood negative to microscopic examination 173 gave a negative result. Of 267 patients with various bacterial and protozoan infections and 91 presumably normal persons, 31 gave a positive complement fixation test. Coggeshal using a similar antigen diluted 1/100 in saline to avoid anti-complementary effect and a test carried out as for Wassermann reaction found that the serum of patients with *P. vivax* and *P. falciparum* malaria fixed complement with the monkey parasite antigen in approximately the same dilution as did those infected with *P. knowlesi*. Kligler and Yoeli using a dilution of 1 in 160 found that the serum of patients undergoing treatment by induced malaria usually gave a positive complement fixation test during the third week after they had had two or more attacks. Patients who were cured after one attack failed to give a positive result. The same authors record cross reactions using antigens of *P. knowlesi* and *P. gallinaceum*. Eagle, Mays, Hogan and Burney used an antigen made from cultured spirochaetes. Although it was an extremely sensitive test for syphilis it did not, in 127 specimens collected after malaria inoculation, permit of differentiation of syphilis from malaria.

CLINICAL PICTURE

Incubation

In Plasmodium vivax infection

Prolongation of the apparent incubation period from infection in the autumn to the attack next spring, or in the case of experimental or induced malaria at approximately a 9-month period after infection, is an important character of *P. vivax* infection, as also is the long period during which relapses continue. Nikolajev records observations in more than 10,000 naturally acquired malaria cases in Lenin-

grad, 9,464 of these were *P. vivax* infections of which 5,220 showed protracted incubation period. Among 200 cases of induced malaria the longest relapse period in *P. vivax* was 27 months, in *P. falciparum* 20 months, and in *P. malariae* 4 years. The relapses in the first mentioned infections followed at short intervals for the first 2 or 3 months and then between 8 and 13 months (long period relapses). Two years in most cases showed complete cessation of attacks. The relapses in *P. falciparum* occurred mostly in the 4-6 month period after the first attack, in *P. malariae* they were most numerous in the first 6-8 months, thereafter slowly becoming less. These results are in general accord with what is now recognized as characteristic of *P. vivax* infection, the long incubation period and long period relapses giving rise to the spring epidemic which is one of the most marked features in the epidemiology of malaria in Europe.

The attack

Malaria in the Forces

The importance of malaria not only among the Forces who may be serving or who may have served in many parts of the globe but also among the civil population, cannot be overestimated. After all great wars malaria remains for many years as a major problem in the general practitioner's work. Benign tertian malaria and malignant subtertian malaria are the two most common types. In the former the reproductive cycle of the parasite is typically two days in length, with the familiar temperature excursion peculiar to it. The rigors may be expected to happen at exactly the same time every other day, and if any person is seized suddenly with a temperature which mounts to 106° F, and particularly when this happens in the morning or afternoon, the diagnosis is almost certain to be that of malaria. The end of the attack is characterized by sudden fall in temperature to a subnormal level. If the condition is a primary one it should be borne in mind that the clinical signs may not be apparent until the disease has been established for some weeks, in primary infections especially, and there are various idiosyncrasies to be taken into account.

So far as subtertian malaria is concerned the infected erythrocytes congregate—and therefore the parasites are very condensed—in the capillaries of the internal organs, this accentuates the malarial picture according to the organ or organs most affected. In this type of fever there is a quotidian periodicity but the temperature is not by any means a constant one. A rise of temperature, a pause and then a further rise is common in subtertian malaria (dicrotic rise). Examination of the peripheral blood may not disclose the parasite (Manson-Bahr).

TREATMENT

Prophylaxis

Communal

Measures on board ship—Extremely important are the outbreaks of malaria which occur among merchant seamen, especially in ships visiting West African and other highly malarious ports. A publication by the Ministry of Shipping describes the preventive action that can be taken in such ships and gives methods for preventing mosquito bites, for mosquito proofing of ships, for quinine prophylaxis and for taking other precautions.

Antilarval measures—In addition to the antilarval measures mentioned on page 169 a method found to be successful in Malaya is the covering of shallow watercourses with packed grass and herbage or with leaves of trees with twigs intertwined so as to form a brushwood drain. Of the more direct and much employed ways of destroying larvae are (1) 'sluicing' which, when it can be properly contrived, has been very effective in certain circumstances, (2) various improved methods of applying Paris green (copper aceto-arsenite), which still remains the most effective and practical method of control by direct action, (3) the use of various types of waste products from oil refineries. The efficacy of this last type of oily larvicide is in the main dependent on the spreading properties of the substance on water, the readiness with which it wets and enters the tracheal system of the larva, and its additional toxic effect due to the more volatile constituents. All these factors, in addition to cost, must be considered when judging the respective usefulness of larvicides.

Knowles, Parker and Johnson found that phenol larvicides, namely cresylic acid in sulphonated oil diluted 2:30 with water and finely sprayed, were much less effective than was kerosene. Among other forms of larvicide are powdered pyrethrum scattered over water in a proportion of 50-100 grammes per 1,000 litres, especially useful for tanks and other small collections of water (Jettmar). Pyrethrum now being difficult to obtain, Jordan and Silvey have tried the comparative value of certain chemical substitutes. They found paradichlorobenzene to be a stable addition to pyrethrum larvicides, allowing of reduction in the amount of pyrethrum in such mixtures, used alone it was the best substitute. It was, however, difficult to dissolve in bulk. Tetralin (tetrahydronaphthalene) was also a useful addition but was dearer, although cheaper than pyrethrum. Trichlorethylene was found to be

toxic to fish and birds Chopra, Roy and Ghosh¹ found the essential oil of *Artemisia* in India to have insecticidal and larvicidal properties comparable with those of kerosene The same authors² found that, although the essential oils of wild species of *Ocimum* in India, Burma and Ceylon had some insecticidal properties, these did not compare with pyrethrum

War-time needs have intensified the efforts to abolish malaria, and nowhere has the activity been so great as in the Army of the United States of America More and more reliance is being placed on the spraying of houses as an antilarval measure In the American Army the Freon bomb, a type of self-propelling insect spray, is employed The contents of this bomb are 20 per cent pyrethrum dissolved in Freon 12 at a pressure of 85 pounds to the square inch There is a nozzle on the bomb and when it is unscrewed a fine spray is set up which is alleged to kill all flies and mosquitoes in a space of 100,000 cubic feet In South Africa village houses are sprayed at a cost of 4d per head per year When possible pyrethrum is grown locally so as to provide material to be used in the sprays

The general principles of prophylaxis against the mosquito are the establishment of mobile malarial laboratories under specialists and the widespread use of mosquito nets and insecticidal sprays, and very thorough supervision and control of breeding grounds of known mosquito carriers

Measures against adult mosquitoes—Of measures directed against the adult insects the spraying of huts has been strongly advocated, especially in some parts of tropical Africa Methods of spraying have also been greatly developed as a means of preventing transport of infected mosquitoes by airplanes, the whole interior of the plane being sprayed by suitably arranged self-acting sprayers, a non-inflammable insecticide being used

Russell and Knipe have described how they have effectively dealt with the spraying of houses in a Madras village The mixture they used consisted of pyrocid, 1 part, kerosene, 19 parts Half a pint of the mixture was used for every 10,000 cubic feet of space, and the house was sprayed outside and inside

Personal

Medicinal—Methods of medicinal prophylaxis have received particular attention in the last few years The report of the Malaria Commission of the League of Nations indicates the general principles involved and the dosage and method of administration desirable The report also enables a comparison to be made between the efficacy of the new synthetic drugs and quinine as shown by a large series of experiments carried out in various countries at the League's suggestion In medicinal prophylaxis a distinction must be drawn between drugs which can be used to prevent infection by destroying the sporozoites before these reach the trophozoite stage, that is so-called 'causal' or 'causative' prophylaxis, and those which act merely by controlling the appearance of active manifestations of infection in the form of clinical attacks of the disease Although theoretically the former is an important objective, it is, with the drugs available, scarcely practicable, since the dosage necessary (for example with plasmoquine (pamaquin)) is too near the possible toxic dose Medicinal prophylaxis is therefore at present almost entirely a matter of controlling, rather than preventing, infection, and the usefulness of different drugs largely depends upon their relative efficacy in this respect in moderate dosage and the degree of safety which attaches to their use in different circumstances These considerations as given in the Malaria Commission's Report are very briefly summarized as follows A daily dose of 0.5 gramme of quinine hydrochloride sometimes causes temporary disappearance of *Plasmodium vivax* or *P. malariae* A dose of 1.0 gramme daily for from 5 to 7 days is often necessary for the above purpose and to tide over a first relapse at some subsequent date A dose of 1.3 to 2.0 grammes is necessary in some countries for *P. falciparum* infection A daily dose of 0.3 grain of atabrin (mepacrine hydrochloride) has a slightly more rapid reaction than has quinine in 1-grain doses, and the absence of clinical symptoms is somewhat more prolonged The effect with *P. falciparum* varies with the strain of the parasite The treatment of relapses is more effective than with quinine The spleen rate in treated indigenous communities decreases more slowly, but the effect is somewhat more lasting It produces yellow discoloration of the skin Plasmoquine used in small doses with quinine or atabrin reinforces their action in the case of *P. vivax* and *P. falciparum* It acts on the gametocytes of all three species In general, therefore, the effectiveness of quinine and atabrin is not greatly different, allowing for the larger dose of the former that is necessary

The methods of using atabrin in prophylaxis have been the subject of much investigation The more usual use of the drug in tropical practice is a course of, say, 0.3 gramme daily (given usually in 3 separate doses each of 0.1 gramme) for 5 or at most 7 days (the usual treatment for an attack of fever) followed by a less frequent dosage, for example 0.3 gramme, 1, 2 or at most 4 days a week

Bispham has studied the reports of 49,681 cases in which atabrin has been administered and himself personally administered the drug in 7,915 cases The slowness

of elimination is important. The bowels should be freely opened and kept open by saline cathartics if necessary. Liquids should be given freely during administration of the drug. The toxicity is of small importance.

The small doses of plasmoquine now used do not usually exceed 0.02 gramme, it is employed almost entirely as an adjuvant. Field, Niven and Mitchell administered 0.02 gramme of plasmoquine twice a week for one year to the population in a garden. This did not affect markedly either the general course or the incidence and severity of clinical attacks.

The drug, certuna (dimethyl-amino-oxyquinolyl-amino-butane) (cilonal), which, like plasmoquine, acts upon gametocytes but is much less toxic, has been given in doses of up to 0.07 gramme thrice daily for 7 days without toxic effects (Sioli). Missiroli and Mosna gave 0.12 gramme a day for 6 days without any toxic effects. It appears to be at least as effective as plasmoquine as a gametocidal drug.

A survey of prophylactic measures

The situation with regard to drugs in the control of malaria has been reviewed by Hughes and Murgatroyd. The main points are as follows: (1) Neither quinine nor mepacrine hydrochloride (atebrin) destroys the infected organism completely. (2) As prophylactics these drugs do not shut out the parasites and clinical manifestation of the disease may occur despite their free use. (3) In war-time quinine is in short supply and the only possible substitute is mepacrine hydrochloride. (4) If the acute attack is aborted speedily, this generally means that there is an increased tendency to the recurrence of relapse. (5) In war-time when European troops are temporarily in malarial regions suppressive treatment is inevitable, otherwise military operations may be held up. (6) There has not been any decision with regard to the optimum dosage and spacing of quinine or of mepacrine hydrochloride. (7) Atypical malaria should not be overlooked, it occurs frequently.

Cure

Antimalarial drugs

Newer drugs—With the exception of the drug, certuna, already referred to, no important new type of antimalarial synthetic compound has been put on the market since the article on malaria was published in the *Encyclopaedia* (Vol. VIII, p. 304). A considerable number of names, however, are encountered in the literature relating to drugs used in some countries either identical with, or very similar to, atebrin or plasmoquine. Some new compounds of an entirely different type have also been shown to possess antimalarial properties, for example undecane diamidine and prosectasine, a sulphonamide compound, but at present these have no importance in the treatment of malaria.

Liu, Chang, Ch'uan and Tan describe an antimalarial alkaloid, sinine, obtained from the bark of *Fraxinus malacophylla*, a common tree in Yunnan. They consider it to be as satisfactory as quinine given in a dose of 3 grammes of dried powder (powdered root bark). Thirty-four cases were treated. Obviously the claim has still to be substantiated.

Quinine—Totaquine should contain at least 15 per cent of quinine, totaquine was one of the drugs recommended by the Malaria Commission, League of Nations. Recent work by Seeler, Dusenbery and Malanga has determined the value of cinchona alkaloids. In their effect on malaria quinine, quinidine, cinchonine and cinchonidine are about equal, but quinidine is not so active. A report by Hawking states that when mepacrine is given intramuscularly it is rapidly absorbed and the local necrosis is about one-third as great as that when quinine itself is used.

Atebrin—Atebrin (mepacrine hydrochloride) is now the main drug used in the fight against malaria because when Japan invaded the Dutch East Indies over 90 per cent of the quinine-producing area of the world was captured. According to Meythaler the drug should be given in benign tertian cases in doses of 5 grains daily, but in all but the mildest case of malignant tertian malaria the dose should be 10 grains while there is any pyrexia, the alternative to this is atebrin musonate (mepacrine methanesulphonate) given intramuscularly in 5-grain doses, the atebrin being dissolved in 10 cubic centimetres of distilled water.

Christophers advises that although 5 grains of atebrin should be given daily for a week, the dose should be divided, 1½ grains or 0.01 gramme being given 4 times a day. This course is repeated if need be after a short interval. The only disadvantage of atebrin is that it dyes the skin.

Sulphonamides—The sulphonamides have had extensive trial, all types having been used. In some cases partial success was achieved, but as a general rule the sulphonamides are not successful in malaria, most workers reporting that quinine or atebrin is to be preferred.

Treatment of the attack

The War Office has published notes on the treatment of malaria occurring in individuals returning from service in malarious areas. The standard Army treatment is as follows:

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Days 1 and 2 Quinine bisulphate or hydrochloride 10 grains in solution in 1 fluid ounce of water by mouth 3 times in 24 hours

Days 3, 4, 5, 6 and 7 Mepacrine hydrochloride 0.1 gram tablet 3 times a day swallowed whole with a draft of water after food

Days 8 and 9 No antimalarial drug treatment

Days 10 to 14 Pamaquin 0.01 tablet 3 times a day after food

Quinine dihydrochloride (acid hydrochloride of quinine) or quinine sulphate may be used in dosage of 10 grains, but the former is more unpleasant to taste and the sulphate requires 1 minim of dilute sulphuric acid (B.P.) or 3 grains of citric acid per grain of the salt to effect solution

Manson-Bahr states that in benign tertian malaria the response to quinine when it is administered intramuscularly may be dramatic but a single injection will not prevent relapses

Treatment of chronic malaria—The treatment of chronic malaria, especially cases of splenic enlargement, with small doses of adrenaline (Ascoli's treatment) has been much used in Italy. Casini, however, in a critically treated series did not find that adrenaline activated latent malaria, nor was there any difference between the treated and control groups in respect to size of spleen. Pizzillo¹ on the other hand finds that in cases treated with adrenaline splenic enlargement does not occur, or if splenomegaly is already present it is reduced. The same author² observed a dangerous (pernicious) relapse after adrenaline administration. Voorhoeve for splenomegaly cases gives intramuscular injections twice a day of 2 cubic centimetres iodoquine (a mixture of quinine, adrenaline, iodine and glycerin), 2 cubic centimetres corresponds to 0.5 gramme quinine dihydrochloride. Preparations under proprietary names of complex composition are much in evidence among Italian writers. Nucciotti uses intravenous injections of $\frac{1}{100}$ milligram 'surrenasi', apparently an extract of the whole adrenal gland and vitamin C. Parise uses a preparation called 'amar', said to contain quinine, arsenic, berberina and other components

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Trensz, F (1936) *Arch Inst Pasteur Algér*, **14**, 353
Voorhoeve, H C (1938) *Geneesk Tijdschr Ned-Ind*, **78**, 2681
War Office (1941) *Notes on the Treatment of Malaria occurring in Individuals returning from Service in Malarious Areas* London
Whittingham, H E (1939) *Trans R Soc trop Med Hyg*, **33**, 304
Wolff, E-K (1939) *Trans R Soc trop Med Hyg*, **32**, 707

MALINGERING

AETIOLOGY

Malingering in workmen

1020

The question of malingering by injured workmen was considered at great length by the Holman Gregory Committee in 1920, who reported that 'We are satisfied that the average workman is anxious to return to his work as soon as he is able, and is not disposed to malingering'. The evidence on which this opinion was based is analysed by Wilson and Levy, who strongly endorse this view, which indeed accords with that of most experienced observers.

The present war does not appear to have led to any considerable increase in incidence of feigned illness during the first year. A few cases have been recorded of attempts to evade military service by this means. Ironside has written on simulation of epilepsy, and Edwards suggests that the injection of a convulsant, such as leptazol (cardiazol), might be used in order to test susceptibility to fits, which he asserts to be heightened in real epileptics, but he points out that such susceptibility can be induced by deep breathing, and occurs in hypoglycaemia. It would be a serious 'assault' to adopt any such drastic mode of testing the veracity of a statement. Reliance must still be placed on less spectacular methods, of which perhaps the most valuable is a careful questioning of the patient, a true epileptic will be quite unaware of any details of his seizures, whereas a malingerer will be likely to describe these with a wealth of horrific circumstance.

In no class of case is it more important to preserve a sympathetic and receptive attitude than when dealing with a case of suspected malingering: an impostor will almost always overact his part if he thinks that everything he says is receiving careful attention and is quite unlikely to distinguish between credulity and open-mindedness on the part of the medical examiner.

- Edwards, J F (1940) *Brit med J*, **1**, 868
Ironside, R (1940) *Brit med J*, **1**, 703
Report of Departmental Committee on Workmen's Compensation (Holman Gregory Committee), 1920
Wilson, A, and Levy, H (1939) *Workmen's Compensation*, Vol 1, 'Social and Political Development', London, p 185

MARASMUS

TREATMENT

1021

At the Baby Clinic Hospital, Kensington, marasmic infants have since 1935 been treated with adrenal cortical extract. This was based upon the facts (1) that the features of marasmus resembled those of adrenal insufficiency and (2) that inanition and infections might produce lesions in the adrenals which would lead to deficiency of their secretion. It seemed reasonable therefore to administer cortical extract in

1021

order to enable the infant to utilize the food ingested until the deficiency had been corrected Hislop recorded the case histories of (1) a preliminary series of 5 cases treated with cortical extract in which the results were encouraging, although the dosage chosen appeared from subsequent results to have been too low and (2) a series of 14 patients, 11 of whom responded satisfactorily and gained weight at a greater rate during the administration of eucortone than before the treatment was started or during the intervals between courses The dosage was 1 minim per 2 pounds body weight daily of eucortone, given intramuscularly

Hislop, W A (1938) *Lancet*, 2, 308

MASSAGE

Addenda

In Vol VIII, p 386, add at end of first paragraph 'Highly skilled massage is required to guide the gas through the desired course, otherwise it merely leaks round the adherent parts'

On p 390, 7 lines from foot, after the first word, 'exercise', add 'The extensor of the elbow, the triceps, merely shortens and lengthens It does not need to contract to perform the extension unless there is opposition to the movement'

Corrigendum

The second end reference to Mennell should read

Mennell, J B (1939) *The Science and Art of Joint Manipulation*
London and Philadelphia

MATERNAL MORTALITY

GOVERNMENTAL AND OTHER INVESTIGATIONS

Report of Inter-Departmental Committee on Abortion

1026

The Report of the Inter-Departmental Committee on Abortion—which was appointed by the Minister of Labour and the Home Secretary in May 1937, under the Chairmanship of Mr Norman Birckett, K C—was issued in June 1939 The reference to the Committee was 'to enquire into the prevalence of abortion and the law relating thereto, and to consider what steps can be taken by more effective enforcement of the law or otherwise to secure the reduction of maternal mortality and morbidity arising from this cause', and their inquiry represents the first comprehensive investigation of this difficult subject undertaken by a Government Committee One member of the Committee signed a dissentient Report

The Committee recorded the general impression that the annual number of abortions is between 110,000 and 150,000, of which perhaps 40 per cent are criminal, and conclude that artificially induced abortions, especially when self-procured or procured by an unqualified person in unhygienic conditions, involve greater risk than do spontaneous abortions

The Committee recommended a clarification of the existing law (subject to certain safeguards) to make it plain that the induction of abortion is legal, not only for saving the life of the pregnant woman, but also when its object is to save her health from serious impairment They were strongly opposed on ethical, social and medical grounds to any broad relaxation of the law, and although they would have welcomed the legalization of the termination of pregnancies resulting from rape, if a solution—which they themselves have been unable to devise—could be found to the difficulties involved, they did not consider that any other non-medical grounds should be recognized as a justification for the operation The desire for criminal abortion should be combated by social, economic and educational measures The Minority Report, however, proposed that the operation should be expressly legalized when pregnancy is a result of rape, unlawful carnal knowledge, or incest, or when hereditary disease is likely to be transmitted, or when the woman has previously carried 4 pregnancies to term

The relation of contraception to abortion was examined The majority of the Committee although not prepared to recommend the use of the public health services for the unrestricted dissemination of birth control advice, considered that the present powers of local authorities—under which they can arrange for contraceptive advice to married women to whose health pregnancy would be detrimental—should be more generally exercised, and that their value should not be restricted by too narrow an interpretation of medical grounds Two members recommended that local authorities should be permitted to give advice in their clinics to married persons who desire it on economic grounds The Minority Report recommended an obligation upon local authorities to provide such advice to all married persons who desire it

The Committee recommended (with a reservation by two members) that medical practitioners, as a safeguard against improper practice, should be obliged to notify therapeutic abortions to medical officers of health, if the law is clarified on the lines they propose A minority recommendation was that other abortions should be notifiable for statistical purposes.

MESSAGE—MATERNAL MORTALITY

The Committee referred to the need for adequate institutional accommodation and skilled professional attention, if ill effects after abortion are to be minimized. They suggested that a suitable opportunity should be taken to amend the Midwives Act, 1936, to secure that the service of midwives which a local supervising authority must provide in its area should be such as to ensure a sufficient number for attending cases of abortion requiring skilled nursing. Among other recommendations, the Committee made suggestions for facilitating the enforcement of the law and for placing further restrictions on the supply and advertisement of abortifacient drugs.

THE PROVISION OF MIDWIVES

The Rushcliffe Committee Report

In the report of the Rushcliffe Committee on Nurses' Salaries (February 1943) it was stated that a separate Committee, also with Lord Rushcliffe as Chairman, was considering midwives' salaries. The latter Committee has reported and its chief recommendation is that State-certified midwives shall be paid according to national salary scales. A schedule of the salaries suggested is given in the report. In making this recommendation the Committee has been mindful of the need for making the midwifery service attractive enough to prevent young midwives from leaving it for the nursing service. The report, in fact, covers more than the question of salaries. Its recommendations include the giving of a uniform, arrangement for transport, holidays and sick pay comprehensive enough greatly to improve the living conditions and therefore the work of the midwife whose duty it is to attend confinements in the homes of her patients, the establishment of hostels or furnished living accommodation for midwives, with attendance and a telephone, in order to relieve them of domestic cares, arrangement for off-duty times. For the midwife working in hospital, similar gains are proposed. In order to attract entrants, all fees from pupil midwives should be discontinued and some payment made during the period of training.

A corresponding Committee in Scotland, under the chairmanship of Professor T. M. Taylor, has made similar recommendations, and local and hospital authorities in Scotland have received the same assurance as those in England and Wales that the Government would pay 50 per cent of any increased expenditures these improved salary scales would mean.

STATISTICS

Rates of maternal mortality in England and Wales

The infant mortality rate for 1942 of 49 per thousand live births registered in England and Wales compares with 59 in 1941 and is the first rate below 50 ever recorded. The increasing number of births tends, however, to depress the crude rate slightly, and the corrected rate based on the number of infants who were actually at risk may, when available, be fractionally above 50. The corresponding infant mortality rates for Scotland were 82.7 in 1941 and 69.3 in 1942. For England and Wales the maternal mortality rate of 2.47 per total thousand births compares with 2.76 in 1941, the deaths from infection during childbirth falling from 0.47 to 0.42 per thousand total births, which is another low record. The corresponding maternal mortality rates for Scotland were 4.7 in 1941 and 4.0 in 1942.

Rates of maternal mortality in other countries*Maternal mortality in Europe*

In Germany infant mortality has not increased. The children receive special nutritional care and are given supplies of vitamin C. The supply of milk to expectant mothers and children is regular and good. These mothers also receive a preparation of vitamin D through the district nurses. Far otherwise is the picture in the occupied countries. As regards nutrition, Poland, Jugo-Slavia, Greece and occupied Russia are in a desperate plight. The 'hungry countries' are Belgium, France and Norway. Czecho-Slovakia is considered to be a little better off. In all the occupied countries pregnant women are inadequately nourished, and it is alleged that a second pregnancy is tantamount to maternal suicide.

PREVENTION OF MATERNAL MORTALITY

Antenatal care*Vitamin supplements*

In November 1942 the Minister of Health issued a special appeal to welfare authorities to do everything possible to secure an increased consumption of these supplements. The Minister of Food at about the same time appointed a Marketing Officer for the purpose of securing a wider distribution of the supplements, and the two departments undertook an extensive publicity campaign with the object of impressing on mothers the importance of giving cod-liver oil and fruit juices to their children. In spite of the many calls upon their staffs, welfare authorities continue to give willing cooperation to the local food control committees, and the Women's Voluntary Services and the National Federation of Women's Institutes readily agreed to help to meet difficulties in rural areas. In addition, many welfare authorities

ties provide meals for necessitous expectant mothers at recognized communal centres

Milk and midwifery

The adequate nutrition of pregnant women is highly important in the interests both of the mother and of her offspring. As is well known, one of the most valuable means of ensuring this is the addition of milk to the ordinary diet, and for a number of years the Ministry of Health has encouraged the supply of milk through maternity centres to expectant mothers as one of the means of prevention of maternal mortality. It has now become a measure of war-time policy. In June 1940 the Minister of Food announced in the House of Lords that he had decided to institute a national scheme for the supply of milk, either free or cheap, to all expectant and nursing mothers and to children under 5 years of age. Under the scheme, which became operative in July 1940, 1 pint of liquid milk—or in special circumstances for children under 1 year of age an equivalent amount of dried milk—is supplied daily to each member of these classes on whose behalf proper application is made.

Emergency units

Supply of transfusion fluids for maternity cases

Most of the pre-war arrangements for blood donor panels and transfusion service generally have been coordinated under the Emergency Blood Transfusion Services. In November 1942 the Minister issued a Circular (No. 2712) to welfare authorities in England outlining the arrangements he has made for the resources of the Services to be available for all maternity cases in which the need for transfusion arises. No charge is made to welfare authorities for the fluid supplied or the apparatus lent by the Emergency Blood Transfusion Services, but authorities are expected to make their own arrangements for transport. Incidentally, expenditure on transport and on the administration of such aids may properly be regarded as an extension of existing maternity and child welfare arrangements under Section 204 of the Public Health Act, 1936.

Postnatal care

Statistics

The increased attendance at antenatal clinics indicates that expectant mothers are becoming increasingly aware of the importance of antenatal supervision, a circumstance which is of the utmost value in combating maternal mortality. The following figures show that the value of postnatal care is still insufficiently appreciated. In 1942 there were 757 postnatal clinics open in England and 7 in Wales, giving a total of 764 clinics as compared with 707 in 1941. There were also 105 postnatal clinics provided by voluntary associations. Thus, while there is some commendable increase in the number of these clinics, it is still insufficient for the country as a whole. The number of gynaecological clinics, which would help to abolish much suffering and disability in women after childbirth, is still far below what is required.

Home helps

In an attempt to help mothers whose conditions of living are such that their confinements can suitably take place at home, Circular No. 2729 was issued (23rd November 1942) to welfare authorities. In this they are urged (1) to provide 'home helps' to give assistance in the home at the time of and during the period of two weeks immediately following the confinement and (2) in places in which such arrangements are already in operation, to extend the scope of the help given. The Circular was accompanied by a Memorandum which summarizes details of existing schemes and gives useful information about the conditions of service and about the pay and duties of home helps as well as about other financial and general administrative matters. The Minister of Labour and National Service agreed to assist welfare authorities, through the medium of his local offices, to obtain suitable women as home helps. By means of such a service it is hoped to reduce considerably the acute pressure on institutional accommodation for maternity cases. In some areas, however, it is not possible to find a sufficient number of women of the right kind to undertake the duties.

MEASLES

AETIOLOGY

Age incidence

1027

Although young people are especially vulnerable, those who are debilitated or who are already affected with respiratory or gastro-intestinal diseases are more susceptible than others are. Lack of vitamins is another strong influence in the aetiology of the disease. So far as adults are concerned pregnancy may increase the vulnerability.

Bacteriology

In the diagnosis of doubtful cases of measles methods of growing virus are not as a rule available and the practitioner is left with Koplik's spots as his only signals, very often these have faded by the time he is called in. The presence of Turck cells

and plasma cells in the blood is a sign of measles, more especially in adults, but it is stressed that rubella also gives the same reaction

Virus infection

Evidence that measles is due to the action of a virus is adduced by Marotta, who claimed to have isolated 2 strains by intratesticular inoculation of measles blood into guinea-pigs which underwent an experimental attack, as they were found to be insusceptible to further inoculations. Immune blood of convalescent human beings and of guinea-pigs was also found to protect guinea-pigs against intratesticular inoculation. Successful isolation of measles virus on the chorio-allantoic membranes of chick embryos is claimed by Rake and Shaffer, in young monkeys which were inoculated with the cultivated virus, experimental measles similar to that described by other workers was produced, and conferred immunity against subsequent inoculations. Later (Stokes and Rake) human beings were inoculated, intranasally and subcutaneously, with the attenuated virus and immunity developed.

Over 150 strains of measles virus were grown on chorio-allantoic membrane by Mayer, who obtained consistently positive results with measles material. Lesions were transmitted serially through a number of egg passages even when diluted membrane suspensions were employed. Cultivation could not be maintained indefinitely as the virus tended to die out after numerous passages. Using the egg method, the virus could be neutralized by measles convalescent serum but unneutralized virus cultures were non-infective for children however they were inoculated. In inoculated subjects the natural disease subsequently developed although 5 of them had atypical attacks.

CLINICAL PICTURE

Complications

Of 8,351 cases of mild measles Chinner found that 9 patients were attacked by encephalo-mylitis at an average interval of 4 days from the onset, 3 died, 3 recovered completely, and the remaining 3 were left with sequelae for at least 6 months. Two were unable to sit up or to speak, of these 2 patients one improved but the other became spastic. The third case was characterized by atrophy and atony of the skeletal muscles.

TREATMENT

Prophylaxis

The most susceptible age group is that of 1-6 years (Thalhimer) and larger doses of immune serum are required for children between these ages than for older children or for infants, for protection 5 cubic centimetres of convalescent serum is recommended for infants, 10 cubic centimetres for children between 1 and 10 years, for those over 10 years a dose of 1 cubic centimetre is given for each year of age. Blood from late convalescents (5-22 months after attack) or pooled ascitic fluid concentrated to half its volume was found to have the protective efficiency of one-quarter the volume of recent convalescent serum.

In a large-scale investigation (Lyall and Murdick) with immune measles globulin (human), 93.5 per cent of those inoculated were protected or acquired the disease in a mild form. A dose of at least 5 cubic centimetres was needed to give protection, about the same as that usually recommended in the case of convalescent serum. At the site of inoculation there was pain and swelling in a quarter of the number of patients and about 4 per cent had fever or malaise.

Serious complications of measles are more to be feared than is the disease itself. Conditions such as panophthalmitis and cancrum oris are now less common as the result of better nutrition and hygiene. Increasing attention is being given to the prevention of infection and cross infection in hospitals, there is more isolation and more space. The oiling of floors and of fabrics and the keeping down of dust generally have had good results, air-conditioning and atmospheric purification by aerosols or ultra-violet radiation have been reported on favourably, but under war conditions are not practicable. Convalescent serum and immune globulin (placental extract) are both of topical interest and their uses in prophylaxis are proved. Toxic hepatitis may be a complication after the giving of convalescent serum. If, however, the donor is carefully selected and the serum collected properly, convalescent serum should confer one hundred per cent protection. It should be given as follows: children under 3 years of age, 5 cubic centimetres, then multiply the age by 2 until the dose reaches 20 cubic centimetres, the dose should be given on or before the fifth day after exposure.

Chinner, M. E. (1940) *Med J Aust*, **2**, 526

Lyall, H. W., and Murdick, P. H. (1941) *N Y St J Med*, **41**, 452

Marotta, G. (1939) *Rif med*, **55**, 1507

Mayer, J. B. (1941) *Arch Hyg, Berl*, **126**, 285

Rake, G., and Shaffer, M. F. (1940) *J Immunol*, **38**, 177

Stokes, J, Jun, and Rake, G (1940) *Science*, 92, Supplement (Sept 20), p 10
Thalhimer, W (1940) *Canad publ Hlth J*, 31, 51

MEDIASTINUM DISEASES

CLASSIFICATION

Traumatic lesions

Aetiology and morbid anatomy

1028

Mediastinal emphysema —As mentioned in the *Encyclopaedia* (Vol VIII, p 439) the causes of mediastinal emphysema are various, and apart from trauma inflammatory disease has always to be borne in mind as a possible cause In 1934 and 1937 Hamman described a condition of what is now well recognized as spontaneous emphysema, or Hamman's disease The characteristics of this condition are sudden severe pain while the patient is resting or at least is not engaged in any great bodily activity, increased resonance over the affected area and 'boiler-like' sounds of loud intensity The last disappear quickly, their place being taken by a few crackling noises In Hamman's disease when air reaches the mediastinum there is pain, which may be very acute, but there is not any shock A peculiar and distinctive sound over the heart is described, this being synchronous with muscular contractions and heard during systole only, rarely it is to be heard during diastole only The area of cardiac dullness may be diminished or completely obliterated and pneumothorax is common In infants the outlook is uncertain and sudden death should always be kept in mind as a possibility Cyanosis occurs in a certain number of cases In the event of there being increasing dyspnoea and cyanosis aspiration should be resorted to, this may relieve the symptoms very speedily

Hamman, L (1934) *Ann intern Med*, 8, 417

— (1937) *Trans Ass Amer Phys*, 52, 311

MEDICAL WITNESS

COURT PROCEDURE

Hearsay evidence

1029

The Evidence Act of 1938, which came into force on 1st September 1938, extends the latitude already given in the courts to the admission of secondary or hearsay evidence It provides for the admission of documentary evidence as to facts which are in issue in a case, any statement made by a person in a document which tends to establish such fact is now, on production of the original document, accepted by the court as evidence of that fact, providing certain conditions are kept These are that (1) the maker of the statement must have had personal knowledge of the matters dealt with or (2) the document is one made by a person in the normal routine of keeping records in his professional capacity or (3) the maker of the statement is also called as a witness in the case, in cases in which the witness would have been called had he been alive but is now dead or bodily or mentally unfit, a document made by him is admissible, provided it can be proved that he actually made it

MEDICO-LEGAL EXAMINATIONS AND REPORTS

Corrigenda

In Vol VIII, p 466, 7 lines from foot of page, for '1938' read '1939' On p 467, line 16, for '1938' read '1939'

Addendum

On p 468 the following two additional scheduled industrial diseases should be added to the end of the list

29 A localized new growth of the skin, papillomatous or keratotic, due to mineral oil, affecting a workman employed as minder or piecer in connexion with the process of cotton spinning by means of self-acting mules

30 Poisoning by diethylene dioxide (dioxan) or its sequelae

MENINGITIS

TUBERCULOUS MENINGITIS

Aetiology

1037

Engel, Stern and Newns have again emphasized the importance of the abdominal route of tuberculous infection in children, and the consequent importance of prophylaxis In 3,214 necropsies at Great Ormond Street Hospital for Sick Children, London, there were 284 (8.8 per cent) cases of tuberculous meningitis, in 41 of these (14.4 per cent) the primary infection was abdominal Of these 41 cases, 28 (67 per cent) occurred between the first and second years of life, there were 4 in the first year, 2 between 2 and 3 years of age, 4 between 3 and 4 years, and 3 between 4 and 5 years In only 4 cases did the condition last longer than 2 months, and in 3 of these there were obvious signs of peritonitis

Engel, S, Stern, R O, and Newns, G. H (1938) *Brit med J*, 2, 1038

AETIOLOGY AND PATHOLOGY

Germ-plasm defect

Penrose, dealing with the genetics of mental deficiency, showed that certain disorders in which amentia was prominent were certainly due to Mendelian characters. Thus juvenile amaurotic family idiocy, phenylpyruvic amentia, familial microcephaly, and probably the Laurence-Moon-Biedl syndrome fitted in with the criteria which point to a single rare recessive gene, whereas epiloia (tuberous sclerosis) was almost certainly a dominant character.

1045

CLINICAL TYPES

Mongolism

Aetiology

Brain changes—Meyer and Jones have carried to a further stage the histological investigations of the brain in mongolism which was published by Meyer and Cook in 1937. In 10 cases of mongolism they describe remarkable brain changes which consisted for the most part of widespread proliferation of the fibrous glia. This overgrowth was largely in the pons and the medulla, and was either diffuse or circumscribed. It was of a distinctly perivascular nature and was best seen with Holzer staining. The myelin and the cell picture often showed no corresponding changes. No common factor was discovered which could account for the changes described. It is suggested that the incidence of pathological changes is greater in mongolism, owing to the peculiar constitution of the mongol, but that they are accidental rather than inherent. It is shown that the findings do not represent the pathological substrata underlying mongolism.

1047

Benda¹, in a series of studies of mongols, comes to the conclusion that the condition appears to be due to 'a congenital absence or deficiency of hypophyseal or extra-hypophyseal agents which simulate differentiation and growth'. He finds changes in the thyroid gland which he believes to be secondary and to point to a pituitary lesion. In a study of 13 pituitary glands from mongols he finds increase of eosinophils and decrease of basophils without pituitary enlargement. He considers this to be pathognomonic of mongolism. In another paper² he shows that the mongol's defective skull is associated with absence or insufficiency of proliferation of the cartilage. In a paper³ dealing with the central nervous system in mongolism he confirms the findings of Meyer and Jones and finds in mongoloid brains of patients between the ages of 6 and 15 years diffuse dropping out of nerve cells, thinning of the first layer of the cerebral cortex with marked patchy demyelination and underdevelopment of the white matter. In two patients aged 20 and 30 years there were marked cortical atrophy and degenerative changes. In infants under one year of age he found advanced oedema of nerve cells with vacuolation and watery dissolution of protoplasm, dropping out of nerve cells and patchy demyelination of the white matter. His observations indicate a progressive degenerative process which in his opinion is due to humoral pituitary deficiency.

Himwich, Fazekas and Nesim, however, veer to the opinion that mongolism may be bound up with a failure of cerebral enzymatic systems (paralleled by the lack of vitamin B complex in pellagra and in beri-beri). They are led to form this tentative hypothesis by the discovery of a significant diminution of cerebral metabolism in both mongolism and phenylpyruvic amentia which is evidenced by decreased cerebral oxygen uptake and decreased utilization of blood sugar by the brain.

Phenylpyruvic amentia (phenylpyruvic oligophrenia)

This rare metabolic disorder was first described by Folling, who reported on 10 children in whom excretion of phenylpyruvic acid and mental defect were associated. Later Folling and Closs reported the presence of 1-phenylalanine in the urine of 4 patients and in the serum of 2. Jervis¹ in the United States of America reported on 50 cases under his observation. The syndrome was characterized by the excretion of phenylpyruvic acid in the urine, pronounced intellectual defect and neurological symptoms consisting of extrapyramidal manifestations and exaggeration of deep reflexes. Jervis considered that the condition is determined by a single recessive gene. Penrose also regarded the disease as due to a recessive gene.

Jervis suggested that the condition was caused by an inhibition in the metabolism of phenylalanine. In a subsequent paper², describing experiments in which subjects of the disease were fed with various pure amino-acids and with phenylpyruvic and phenyllactic acids, he confirmed this view and concluded that the subjects were unable to oxidize the keto acid at a normal rate and therefore excreted it in excessive amounts in the urine.

Benda, C. E. (1939)¹ *Arch. Neurol. Psychiat.*, **41**, 1, 83

— (1940)² *Amer. J. Path.*, **16**, 71

— (1940)³ *Amer. J. ment. Def.*, **45**, 42

Folling, A. (1934) *Hoppe-Seidl Z.*, **227**, 169

— and Closs, K. (1938) *Hoppe-Seidl Z.*, **254**, 115

CUMULATIVE SUPPLEMENT 1945

- Himwich, H E, Fazekas, J F, and Nesin, S (1940) *Amer J ment Def*, 45, 37
 Jervis, G A (1937)¹ *Arch Neurol Psychiat*, Chicago, 38, 944
 — (1938)² *J biol Chem*, 126, 305
 Meyer, A, and Jones, T B (1939) *J ment Sci*, 85, 206
 Penrose, L S (1938) *J ment Sci*, 84, 693

MENTAL DISEASES, HEREDITY

HEREDITARY MENTAL DISEASES

1059

Schizophrenia and manic-depressive states

The hypothesis that the inheritance of schizophrenia depends upon a single recessive gene is not altogether supported by recent reports

Elsässer examined 28 families in which both parents were psychotic. These families combined a total of 106 children, 47 per cent of whom were affected. In 10 cases both parents were schizophrenic, 50 per cent of their children were schizophrenic. In 6 cases one parent was schizophrenic and the other manic-depressive, 46 per cent of their children were mentally affected. Of the children of 2 pairs of manic-depressive parents, 65 per cent were affected. In 10 cases the parents suffered from an atypical psychosis and 47 per cent of their children were mentally affected. Half the number of children who were not mentally affected were strange mentally. Of the grandchildren 10 per cent were psychotic and half the number of the unaffected grandchildren were either schizoid or unstable. Among the 18 adult great-grandchildren 6 are strange but psychosis has not so far been observed in them. In one family in which the father was affected at the age of 17 by hebephrenic catatonia and the mother by stuporous catatonia, 5 of their 6 children are hebephrenic-catatonics and the other is schizoid.

Schulz examined 1,257 adult offspring in 386 families in which the parents were either psychotic or had close relatives mentally affected.

(1) In 141 cases both parents were mentally affected. These were divided into 2 groups. (a) The parents were either both schizophrenic, one schizophrenic and one manic-depressive, or both manic-depressive. In this group the probability of the children being psychotic was very great, particularly when both parents were schizophrenic. (b) Among the parents in this group, either (i) one parent suffered from depression resulting from involution or senile or presenile melancholia, or (ii) one parent suffered from induced mental disease and the other from schizophrenia or litigation mania. In this group there was less tendency for the offspring to be psychotic.

(2) In 84 cases one parent was mentally affected, the other parent was not affected but had a mentally affected brother or sister. The children in this group were less likely to be psychotic than were those in group A.

(3) In 161 cases neither parent was mentally affected, one parent, however, had an affected brother or sister and the other parent had an affected parent, brother, sister, half-brother or half-sister. In this group the proportion of affected children was less than in groups 1 and 2.

The author concluded that these figures support the view that schizophrenia and manic-depressive psychoses are inherited as dominants.

Slater investigated the psychological constitution of the parents and children of 315 manic-depressives. The incidence of manic-depressive psychoses in the parents and children was 11.5 per cent and 22.2 per cent respectively, the incidence of schizophrenia 0.8 per cent and 3.1 per cent respectively. A survey of the literature shows that the incidence of manic-depressives is 0.38 per cent. As regards the type of inheritance, Slater thinks the evidence points to a sex-linked factor.

Ziehen criticized the hypothesis of a recessive factor and put forward a complex hypothesis of a dominant specific factor coupled with a dominant inhibiting factor, schizophrenia developing only when the inhibiting factor is absent.

Galatschyan has investigated the families of 214 schizophrenics, altogether 6,030 persons, and finds a rather higher incidence of schizophrenia in the blood relatives of schizophrenics than previous authors have found. He tends to support the monohybrid recessive inheritance of schizophrenia.

PSYCHOPATHIC PERSONALITY

Inheritance

1060

Brown, in a communication to the Psychiatric Section of the Royal Society of Medicine, reported on the results of an investigation into the family histories of a group of patients who were suffering from anxiety states, hysteria and obsessional neurosis. He also investigated a group of control patients. Inquiries were made about both first and second degree relatives, and in general the work was very thoroughly done, a large proportion of the relatives being interviewed personally. The patients themselves were evenly distributed in their families and there was not any indication that birth order was of any significance in the production of

neurosis. This is rather against great importance being attached to birth trauma as a cause of neurosis or to psychological differences in the family in the attitude of parents to first, last or only children. The two following tables summarize the results in the first degree relatives

TABLE I—Psychiatric abnormalities in parents

				ANXIETY STATES	HYSTERIA	OBSSESSIONALS
				%	%	%
Anxiety states	-	-	-	21.4	9.5	—
Hysteria	-	-	-	1.6	19.0	—
Obsessional neurosis	-	-	-	—	—	7.5
Depression	-	-	-	5.6	—	7.5
Anxious, depressive or obsessional personality	-	-	-	17.5	14.3	32.5

TABLE II—Psychiatric abnormalities in siblings over 15 years of age

				ANXIETY STATES	HYSTERIA	OBSSESSIONALS
				%	%	%
Anxiety states	-	-	-	12.3	4.6	5.3
Hysteria	-	-	-	2.2	6.2	—
Obsessional neurosis	-	-	-	0.9	—	7.1
Depression	-	-	-	0.9	—	1.8
Anxious, depressive or obsessional personality	-	-	-	16.7	6.2	9.6

The most striking point about the above tables is that they show a considerable degree of specificity between the three types of neurosis. Relatives of persons who are suffering from anxiety states tend to suffer almost exclusively from similar conditions and their susceptibility to hysteria and obsessional neurosis is scarcely more than the average. *Mutatis mutandis*, the same is true of hysteria and obsessional neurosis. The one exception to this is the high incidence of depressive states in the parents of obsessionals. The individuals included under anxious, depressive or obsessional personality could not be conveniently divided in smaller groups, and this is probably the reason why the large proportion of psychiatrically abnormal relatives of obsessional neurotics are included in a group of abnormal personalities rather than in a group of the actually ill subjects. Brown is inclined to interpret the findings as negating any simple Mendelian inheritance in the neuroses but as practically conclusive of the significance of hereditary factors. There are probably a great number of these which can act in a cumulative way and it is possible, especially in view of the high incidence rates in the parents, that a number of them are dominant in type.

Brown, F (1942) *Proc R Soc Med*, **35**, 785

Elsasser, G (1939) *Z ges Neurol Psychiat*, **165**, 108

Galatschjan, A (1937) *Schweiz Arch Neurol Psychiat*, **39**, 291

Schulz, R (1939) *Z ges Neurol Psychiat*, **165**, 97

Slater, E (1938) *Z ges Neurol Psychiat*, **163**, 1

Ziehen, V (1937) *Arch Psychiat Nervenkr*, **107**, 1

MOUTH DISEASES

Addenda

In Vol VIII, p 624, 4 lines from foot of page, after the sentence ending in 'render diagnosis difficult', add: The vesicant gases when inhaled through the mouth, or introduced in contaminated food or drink, cause acute inflammation of the mucosa, sometimes with fibrinous exudate, haemorrhage, necrosis and later atrophic changes. In the acute stage of lesions due to chlorarsine and mustard, rinsing the mouth with 1 in 1,000 potassium permanganate or 5 per cent sodium bicarbonate is recommended. Sedatives are useful, but morphia should be given with caution (Eckert-Mobius).

On p 631, at the end of the paragraph on *Pellagra* add: An epidemic form of glossitis occurring in Palestine, possibly allied to pellagra, is favourably affected by the administration of nicotine acid, 50 milligrams, 4 to 6 times a day for a long period.

On p 637, at the end of the second paragraph under *Exfoliative glossitis* (*Geographical tongue*), after the sentence ending in 'unsatisfactory', add: A painful form with localized burning sensation has been described.

On p 656, at the end of the second paragraph, after the sentence ending in 'mandible', add: Ewing's tumour also occurs within the bone of the lower jaw.

Tabor, S H, and Newman, B (1940) *Arch Pediat*, 57, 133
 Volpe, A (1939) *Arch Pediat Uruguay*, 10, 406

MUSCLE DISEASES**INJURIES****Tenosynovitis stenosans****1093**

Although this condition has been described on numerous occasions in foreign journals, it has received little recognition in Great Britain. It was originally noted in 1895 by de Quervain, and in 1930 Finkelstein reviewed the condition. The patient complains of difficulty in gripping small objects, and of pain over the lower end of the radius, often extending up the forearm. On examination there is a tender swelling of the sheath of the abductor longus and extensor brevis tendons, abduction of the thumb and ulnar deviation of the wrist cause considerable discomfort. The condition is often diagnosed as 'arthritis' of the wrist, and the thickening of the tendon sheath may be so cartilaginous that it can be mistaken for a bony exostosis.

Aetiology

In a series of 12 consecutive cases, 10 occurred in women and one was bilateral. In all cases the patient's occupation was one in which the fingers and thumb were used to an extreme degree, during work as a seamstress, typist or professional fencer, who is accustomed to grip the foil between the thumb and forefinger.

Histology

In severe cases the synovial layer is completely destroyed, the loose connective tissue layer is compressed and thinned, and the ligamentous layer is markedly thickened and undergoes hyaline and cartilaginous transformation.

Treatment

There is never any difficulty in persuading the patient to undergo an operation to relieve the condition. Under local anaesthesia with 2 cubic centimetres of novocain, a 1½-inch incision is made over the swelling, the small branch of the radial nerve is easily seen and the sheath is opened above this point, a groove director is inserted and the thickened portion incised until the normal sheath is again encountered. Often there is considerable excess of synovial fluid above the constriction, and immediate increase in the thumb movements is at once recognizable. In order, however, to secure permanent relief from the condition, as much of the thickened area should be excised as possible, incision only is liable to be complicated by a recurrence of the symptoms within 6 months.

Prognosis

Operative treatment gives complete relief within one week, and the only cases which have recurred are those in which the sheath has not been completely excised.

Treatment

Treatment of minor muscle injuries by the injection of procaine hydrochloride (novocain) according to the technique of Leriche is increasing in favour. Leriche discovered that injection of a 'sprained ligament' with 10 or 20 cubic centimetres of 0.5 or 1 per cent procaine hydrochloride (novocain) resulted in permanent cure. Campbell gave several hundreds of injections for acute and chronic sprains of elbows, knees, shoulders and fingers with satisfactory results in all cases but particularly in ankle and knee cases. In acute, not in chronic, sprains acute pain at the site of injection begins exactly 2 hours after the injection, lasts for 4 hours, and then as suddenly disappears, acute cases therefore should not be treated by this method unless they are severe.

Smiley injected 20 cubic centimetres of a 1 per cent solution of novocain into the painful area in the calf in a case of 'ruptured plantaris tendon', the pain was greatly relieved, but the next day a small area of tenderness was still present and 30 cubic centimetres of the same solution was injected, this relieved the pain completely. Smiley considered that if at the first injection the area is injected so thoroughly that pain cannot be elicited by deep pressure or by the stresses it is designed to bear, a second injection should not be necessary.

TUMOURS**Sarcoma of muscles****1099**

Gordon-Taylor quotes an article by Moulouguet and Pollosson which gives figures obtained from Neck's statistics to show the relatively infrequent occurrence of muscle sarcomas. Between 1904 and 1926 Neck dealt with 67 sarcomas of limbs of which 20 only involved the soft tissues. Proof of the myogenic origin of certain forms of muscle sarcoma is given in a picture in Gordon-Taylor's article, which demonstrates the different types of cell which may be found in the rhabdomyosarcoma of skeletal muscle. The age of incidence of muscle sarcomas appears to be most often about 20, 40 and 70 years, although he states that the condition is liable to develop at any age. The sexes appear to be equally vulnerable. As regards mode of origin, it is not clear whether this can be definitely ascribed to injury, but the author quotes

1099

several cases in which a sarcoma of the muscle has clearly developed after an injury Clinically the condition begins as a painless localized swelling often discovered accidentally, and usually there is not any accompanying functional disturbance In the early stages the tumour is single, rounded or ovoid, and often deep seated Prognosis is always very serious, and in the case of a rhabdomyosarcoma very grave The spindle-celled sarcoma does not have such a grave prognosis, and that of the fibrosarcoma is best of all So far as treatment is concerned Gordon-Taylor advocates wide excision or amputation with or without deep X-ray therapy Some surgeons claim good results from excision, radium being left in the wound

Campbell, W G (1938) *J R nav med Serv*, 24, 48

Finkelstein, H (1930) *J Bone Jt Surg*, 12, 509

Gordon-Taylor, G (1940) *Brit J Surg*, 28, 1

Smiley, W K (1939) *Brit med J*, 1, 1138

MYASTHENIA GRAVIS

AETIOLOGY

- 1100 Eaton reports that the relation of myasthenia gravis to thymic abnormalities is established, and advocates radiographical examination of the chest in every case of myasthenia gravis

TREATMENT

An advance of some importance in the treatment of myasthenia gravis is the use of prostigmin tablets given by mouth Each tablet contains 15 milligrams, and the dosage is calculated empirically, depending upon the severity of the case, and varying from one tablet 3 times daily to two tablets every 2 hours With the larger dose tincture of belladonna must be pushed to prevent griping, some authors have claimed that zinc protamine insulin, 10-20 units every morning, augments the effect of the prostigmin On this therapy it is possible to 'stabilize' even severe cases and make the patients relatively comfortable

Eaton reviews the treatment of myasthenia gravis and states that the oral use of prostigmin bromide is the basic treatment for most cases Guanidine hydrochloride and potassium salts in relatively large doses, namely 300-600 grains daily, are used as adjuncts, guanidine has a less vigorous but more sustained action than has prostigmin and the requisite dosage is somewhat variable, it is usually given in 2-grain tablets

Eaton, L M (1942) *Proc Mayo Clin*, 17, 81

MYCOSIS FUNGOIDES

MORBID ANATOMY AND PATHOGENESIS

- 1103 Whittle reports observations on myasthenia gravis, and points out that the pathological concept of mycosis fungoides differs from the clinical concept Pathologically mycosis fungoides is a characteristic type of cutaneous disease due to one or more of a number of lymphoblastomas Typical clinical cases may be any of a number of lymphoblastomas, some are Hodgkin's, and some are reticulum-celled sarcomas Mycotic cells are typical in all cases and these are not present in psoriasis The possibility of an allergic aetiology must be considered in patients who have remissions when in hospital

TREATMENT

Life can be prolonged for a number of years by X-ray treatment, but this is hazardous Irradiation may cause disappearance of the lesions, but they return on the same areas Chaulmoogra oil is said to effect some improvement

Whittle, C H (1942) Personal Communication

MYIASIS

INFECTION OF NOSE, EAR AND EYE

- 1104 It appears that two morphologically similar species have been confused under the designation of *Cochliomyia macellaria* The obligatory flesh-breeding human species should be henceforward named *Cochliomyia hominivorax* *C. macellaria* is solely a carcass-breeding fly In five years, 1928-32, there were treated in hospital in British Honduras, British Guiana and Trinidad 179 cases of myiasis, the majority of which were probably due to *C. hominivorax*

LARVA MIGRANS

Flies involved

Probably, as was originally indicated, there are several causes of creeping eruption, and the form which is known in Natal as 'sand-worm' eruption has been shown by Murray to be caused by a mite, some 300 μ in length, which deposits its eggs in the burrows It appears to be closely related to *Tetranychus molestissimus* which is found in Argentina and Uruguay, where it attacks men and animals

Murray, N L (1939) *Brit med J*, 1, 1026

CLINICAL PICTURE

General signs and symptoms

Blood picture

The blood picture of myxoedema has recently been more clearly established. The characteristic anaemia of the condition is hyperchromic in type, associated with a hypoplastic bone marrow, the result of the general metabolic defect. Sternal puncture shows a reduction of nucleated cells. The colour index is about unity but the anaemia is not severe, the haemoglobin never falling below 60 per cent. The peripheral blood shows some macrocytosis, no poikilocytosis and no excessive anisocytosis. The reticulocyte count, the serum bilirubin and the gastric function are all normal. The anaemia disappears slowly under treatment with thyroid in conjunction with a regeneration of the bone marrow. It is uninfluenced by iron or liver extract.

1111

Renal function

Beaumont and Robertson publish a further study of renal function in myxoedema. Previously they described a case of pituitary hypothyroidism in which renal impairment was a prominent finding. The authors have now investigated 7 cases of myxoedema and observations were made before and after adequate thyroid gland administration. The later observations were made 3 months after treatment was started when the basal metabolism had become constant on a maintenance dose of thyroid extract. It was found that the urea clearance in myxoedema is low, rises after adequate thyroid treatment but still remains subnormal. Water excretion is normal and thyroid treatment does not cause any significant change. Myxoedematous subjects are able to concentrate their urine as efficiently as are normal persons. After thyroid administration the urinary specific gravity is lowered but not apparently as a result of diuresis. Chemical and microscopical urine examination did not demonstrate any other evidence of renal impairment in the authors' cases.

Beaumont, G. E., and Robertson, J. D. (1943) *Brit med J*, 2, 578

NEGLIGENCE, PROFESSIONAL

Corrigenda

In Vol IX, p. 121, in the paragraph on *Statutes of limitation*, the third sentence beginning 'This time' should now read 'This time is shortened to twelve months in respect of actions against public authorities and persons performing statutory duties (Section 21 of the Limitation Act 1939 under the Public Authorities Protection Act) and an action for negligence against the estate of a deceased person by virtue of the Law Reform (Miscellaneous Provisions) Act, 1934, can be maintained only (1) if the proceedings had actually been instituted prior to his death or (2) if the cause of action arose within twelve months of his death and action was begun within twelve months of the grant of probate or letters of administration. In the case of *Nelson and Anor v Cookson and Anor* the Court decided that doctors employed as medical officers in a hospital maintained by a County Council are within the class of persons entitled to the protection of the Public Authorities Act'.

On p. 121, the first paragraph under *The Tribunal* should read 'An action for negligence may be brought in the County Court, but owing to the limit of damages which can be claimed in the County Court, namely £200, it is more usually brought in the High Court. The Administration of Justice (Miscellaneous Provisions) Bill 1938 now having been made law the limit of damages was raised from £100 to £200'. *Mahon v Osborne*, 160 L.T.R., p. 329, *Nelson and Anor v Cookson and Anor*, 161 L.T.R., 346.

LIABILITY FOR NEGLIGENCE

Civil liability

Vicarious liability

With reference to the case of *Hillyer v St-Bartholomew's Hospital Governors* (25 *The Times* L.R. 762 [1909], 2 K.B. 820), the case of *Gold v Essex County Council*, in which important developments occurred, is of the greatest interest. The plaintiff was awarded by the Court of Appeal £300 damages for ulceration of the face which was caused by Grenz ray treatment. This decision has destroyed the old position as it has remained since the *Hillyer* case referred to above was adjudicated.

1125

Defences

The Court of Appeal in the case of *Osborne v Mahon* decided that the doctrine of *res ipsa loquitur* could not be held to apply to a claim for damages for negligence when a swab was found to have been left in the abdomen. The onus is still on the plaintiff to prove conclusively that the surgeon himself actually left the swab in the abdomen, and that his action was negligent.

Reference may also be made to the possibility of vicarious liability should the swab have been overlooked by the negligence of the nursing staff and this may be considered in relation to the two cases *Hall v Lees* (1904), 2 K.B. 602, and *Perionowski v Freeman* (1866), 4 F. and F. 977.

NEMATODE INFECTIONS, INTESTINAL OXYURIASIS

1129 Life cycle of *Oxyuris vermicularis*

By researches made under the auspices of the United States Public Health Service the rather cryptic life cycle of *Oxyuris vermicularis* has been to a certain extent elucidated. At any time from 15 to 28 days after the ova have entered the host's body, the female worms may appear at the anus. An *oxyuris* may be expected to deposit about 11,000 eggs on the skin.

Diagnosis

The use of the special Cellophane swab is now common. This swab, first described by Hall in 1937, is made by folding a square inch of Cellophane over the rounded end of a glass rod and fixing it in position by means of a rubber band. Only about 5 per cent of children in hospital show ova in the stools, whereas nearly 22 per cent give positive results when one swab is used and 42 per cent when 3 swabs are used. In the United States of America it has been shown that if Cellophane swabbing is persisted in, by the time 7 swabs have been taken from an individual 99 per cent positivity is obtained.

Pathogeny and symptoms

It is clear that in the majority of patients oxyuriasis does not cause any symptoms. In one series in which 500 so-called unaffected children were examined by Cellophane swabs, 19 per cent were found to be infected. It is generally agreed that there are three possible groups of symptoms. These are (1) the gastro-intestinal type, (2) the local type with all its irritative manifestations and (3) the nervous type in which disturbed sleep and enuresis are manifest. There can be no denying that from comparisons made with the symptoms complained of by healthy children the use of the Cellophane swab is the only satisfactory method of assessing the symptoms. Threadworms are also prevalent among the general population, for this reason attacks should be dealt with vigorously.

Treatment

A diet of raw carrots, an ancient and popular remedy for threadworms, is extensively employed in zoological gardens to rid monkeys and other animals of this infection.

Wright, Bozicevich and Gordon find that tetrachlorethylene, when administered orally in a dosage of 0.1 cubic centimetre for each year of age and followed by a dose of magnesium citrate, is effective. The oral use of this salt may also be made next morning before an enema is given which contains 1 cubic centimetre of tetrachlorethylene in coconut oil soap solution.

The thiazine dye phenothiazine (phenovis) has been applied in the treatment of helminthic diseases in domestic animals and especially in strongyloid infestations of sheep. Errington discusses a number of cases in which toxic symptoms occurred after administration of phenothiazine to horses, and advocates caution in dosage. The manifestations were anaemia, albuminuria and haemoglobinuria. Phenothiazine has been tested in human helminthic diseases by Manson-Bahr. It gave good permanent results in 6 children and in 3 adults. Confirmation soon came from Canada. Kuutunen-Ekbaum reported upon 89 children and 9 adults with success. Adverse symptoms were not noted. The dye is excreted in the urine which is stained red or pink. It has been found to be specific for oxyuriasis for which it would appear to be the simplest remedy known. It is put up in tablet form, and also in a granular preparation flavoured with lime juice, and is agreeable to children. For the treatment of oxyuriasis the dose should be 0.5 gramme daily for 5 consecutive days for children under 5 years of age, from 5 to 10 years 1 gramme, from 10 to 20 years 4 grammes, above that age 8 grammes. No special preparatory routine or aperient treatment is necessary. In adults in whom the infestation is particularly persistent and resistant, a second course of the drug is usually necessary. The oxyurids killed by the dye are usually stained red.

The use of phenothiazine, however, has been more or less discontinued as it is too dangerous for general use. In a Special Article in the *Lancet* there is a report of a girl aged 6 years who was given a total of 8.5 grammes in a period of 5 days. By this time the child had become pale and yellow, and complained of headache. A blood count showed very severe aplastic anaemia with normoblasts. She died after a blood transfusion, but the appearances of the blood, spleen and marrow were consistent with haemolytic anaemia. From this, and from other evidence which has recently accumulated, it is apparent that phenothiazine is too toxic for general use in children as it exerts a direct effect on the developing bone marrow. Most authorities prefer gentian violet given in special capsules, the dose being $\frac{1}{2}$ -grain per year of age per day for 5 days. There is then an interval of 5 days and then a second 5-day course. D'Antoni and Sawitz report on a study made to determine the efficacy of gentian violet in ridding children of threadworms in New Orleans. Diagnosis was

NEMATODE INFECTIONS—NERVE INJURY AND REPAIR

made by N I H swab, and freedom from infection was admitted when 7 consecutive examinations had been negative. The dosage of gentian violet was from 0.5 grain given 3 times daily to courses of 1 grain 3 times daily for 5 to 8 days, with repetition of course. The cure rate was 90 per cent.

Wright, Brady and Bozicevich recommend hexylresorcinol in the form of a retention enema 1 in 2,000 solution given after a cleansing enema of soap and water, 4 ounces of hexylresorcinol are given to adults, and as much as can be retained to children. One enema every 3 weeks is sufficient. Negative Cellophane sprayer N I H swabs were subsequently obtained in two-thirds of the number of patients after this course. No better results were obtained by simultaneous oral administration of the drug.

De Eds and Thomas, in their studies on phenothiazine, have drawn attention to the biliary excretion and anthelmintic action of thional. The anthelmintic action of the drug is due to the thional excreted into the intestine by way of the biliary tract, and that bile facilitates this action. On oxidation phenothiazine becomes first leucothional and then thional and, when first given by the mouth, all three substances are found in the faeces. Phenothiazine has not any demonstrable action *in vitro* on *Ascaris lumbricoides* from the pig. Thional first stimulates and then depresses the worm, as long as the drug is in adequate concentration and bile is present.

D'Antoni, J. S., and Sawitz, W. (1940) *Amer J trop Med*, **20**, 377

de Eds, F., and Thomas, T. O. (1941) *J Parasit*, **27**, 143

Errington, B. J. (1941) *Vet Med*, **36**, 188

Kurtunen-Ekbaum, E. (1941) *Canad publ Hlth J*, **32**, 308

Manson-Bahr, P. (1940) *Lancet*, **2**, 808

Special Article (1942) *Lancet*, **1**, 86

Wright, W. H., Brady, F. J., and Bozicevich, J. (1940) *Brit med J*, **1**, 535

NEPHRITIS AND NEPHROSIS

MORBID ANATOMY

Glomerulo-nephritis

Differential diagnosis of diabetic renal lesions

Allen states that the renal lesion in diabetes mellitus is a distinct entity, namely a focal intramural lesion, and not intercapillary as was previously supposed, it is easily distinguishable from the glomerulosclerosis of nephrosclerotic kidneys in non-diabetics, of which it has been regarded as being an advanced stage, and from hyalinization of glomerulo-nephritic kidneys.

1134

RELATION OF NEPHRITIS TO HYPERTENSION

The analysis of the chemical mechanism of renal hypertension is unexpectedly complicated, the renal pressor substance may be an enzyme, a globulin in the plasma which, by the action of this enzyme, yields 'hypertensin', an activator of hypertensin and some substance or substances which inhibit the formation or activity of hypertensin (Special Article).

COURSE AND PROGNOSIS

Glomerulo-nephritis

Acute

Evidence of the usually benign character of acute glomerulo-nephritis was given by Murphy and Rastetter who noted that complete recovery occurred in 50 per cent of cases and that in a large number of them hypertension never appeared. At the same time they considered that some permanent damage occurred in all cases.

1136

Allen, A. C. (1941) *Arch Path*, **32**, 33

Murphy, F. D., and Rastetter, J. W. (1938) *J Amer med Ass*, **111**, 668

Special Article (1941) *Lancet*, **2**, 575

NERVE INJURY AND REPAIR

TREATMENT OF NERVE INJURY

Methods available

Many researches have been carried out and many tests have been made of nerve suture. The main lines of treatment in an injured peripheral nerve are those of splintage, physical therapy, occupational therapy and post-operative treatment which is determined on principles the same as those established for pre-operative treatment. Within recent years most of the interest has centred on the surgical treatment of peripheral nerves because of the various possibilities of nerve suture and of repair by other means. A nerve may be sutured as a primary or secondary measure, and nerve grafting has been adopted by certain surgeons. The results of treatment must inevitably be held back until more time has passed in order to allow the surgeons to assess the value of nerve repair, whatever method may be employed. Most experts are agreed that if the two severed nerve ends can be brought together

1144

- 1144 and suture performed, the most satisfactory results are to be expected. If the gap is too big nerve grafts should be used.

A good deal of work has been done in which concentrated plasma has been employed to unite the severed ends of nerves, the plasma clots to a firm jelly and the stumps are held together. Some workers have advocated the use of autologous plasma, others have experimented with fibrin suture.

NEUROSYPHILIS

INTRACRANIAL SYPHILIS

General paralysis of the insane

Treatment

- 1152 *Pyretotherapy*—In a report on fever therapy by physical means authorized by the Council on Physical Therapy of the American Medical Association, Krusen and Elkins report that fever produced by physical methods is as satisfactory as that produced by malaria in the treatment of general paralysis. The number of patients who show immediate clinical improvement is slightly greater with physically induced fever, but some authorities anticipate a greater relapse rate.

Pakenham-Walsh reports that bistovol (the bismuth salt of acetarsol) is a useful adjunct in malarial therapy, it produces relatively few toxic effects and is preferable to tryparsamide and stovarsol on account of its more rapid reduction of the cell count in the cerebrospinal fluid, it may be given by mouth or by intravenous injection.

SPINAL NEUROSYPHILIS

Tabes dorsalis

Diagnosis and differential diagnosis

- 1158 Among the conditions from which tabes dorsalis must be differentiated is that of 'tonic pupils and absent tendon-jerks'. The diagnosis depends chiefly on (1) the peculiar features of the tonic or 'pseudo-Argyll Robertson' pupil (see Vol II, pp 7 and 8), (2) the complete absence in the latter condition of the sensory features of tabes, namely pains and hypalgesia, (3) the absence of ataxy and of Romberg's sign, (4) negative blood-Wassermann reaction and normal cerebrospinal fluid. The differentiation is most difficult in cases of mild tabes resulting in adult life from congenital syphilis, because in such cases the only abnormalities may be pupillary changes and absence of some tendon-jerks. The diagnosis then depends almost entirely upon the state of the pupils.

NEUROSYPHILIS DUE TO CONGENITAL SYPHILIS

- 1166 According to Purdon Martin's observations, and analysis of the records of the National Hospital, London, cases of juvenile tabes fall into two groups. (1) Severe cases, with positive Wassermann reactions, the onset is usually about puberty but may be much earlier, optic atrophy is the outstanding symptom and is associated most commonly with fixed or Argyll Robertson pupils and absence of tendon-reflexes. Mild ataxy and superficial sensory disturbances develop in the course of years and a considerable proportion of the patients become mentally affected and pass into a state of tabo-paresis. (2) The larger group comprises mild cases which are almost always completely Wassermann negative. The patients have, as a rule, reached adult life before any abnormality is observed and in many instances come under observation because of some symptom which is not tabetic. Abnormal pupils and lack of tendon-jerks are then observed. Most of these cases are very slowly progressive and some remain stationary. Optic atrophy may rarely ensue, fits sometimes occur in these patients. In spite of the negative serological tests, antisyphilitic treatment should be given if there is any sign of activity of the disease.

Krusen, F. H., and Elkins, E. C. (1939) *J. Amer. med. Ass.*, **112**, 1689.

Pakenham-Walsh, R. (1942) *J. ment. Sci.*, **88**, 344.

NOSE AND NASOPHARYNX DISEASES

INTERPRETATION OF SYMPTOMS

Durand's disease

- 1168 Under the above title Findlay describes a virus disease which is transmissible to man and animals, especially guinea-pigs, but also to rhesus monkeys, cats, dogs, hedgehogs and Orkney voles. Durand, of the Pasteur Institute in Tunis, isolated the virus, provisionally called the D virus, from his own blood, and very kindly placed the new virus at Findlay's disposal. Findlay describes a case in a laboratory worker (G. M. F.) with fever of 102.6° F., headache, nasal catarrh, cough, nausea and vomiting of altered blood. Complete cross immunity between the G. M. F. strain and the stock strain of D virus was demonstrable in convalescent guinea-pigs. The incubation period in this case was probably less than 8 and not more than 4 days, in most animals it was from 2 to 3 days, but with small doses of the virus the incubation period might be from 10 to 14 days. D virus is comparatively resistant to inactivation by heat, and is cultivated in serum-Tyrodé's solution and chicken

embryo and in the developing chick embryo *in vivo* No cross immunity with lymphogranuloma venereum or lymphocytic choriomeningitis was found
Findlay, G M (1942) *Trans R Soc trop Med Hyg*, **35**, 303

NYSTAGMUS**AETIOLOGY AND PATHOLOGY**

Nystagmus may be due to toxic causes and in particular to barbiturate intoxication In some cases of prolonged alcoholic excess the patients become unable to fix steadily and show with all positions of the eyes a very irregular nystagmus of rather large amplitude which gives them a 'shifty' expression 1169

NYSTAGMUS OF PALATE

Guillain summarized the knowledge gained at the Salpêtrière on the syndrome of synchronous rhythmic palato-pharyngo-laryngo-oculo-diaphragmatic myoclonus, generally known as nystagmus of the soft palate Myoclonus of the muscles of the neck, trunk and limbs has been associated When the eye-balls are affected the myoclonic movements are oscillatory and differ from those of true nystagmus The rhythm of the contractions is always the same in the same patient and in the various organs affected, but varies among individuals from 80 to 180 per minute The author stated that neither scopolamine, stramonium, physostigmine, morphine, nor ergotamine tartrate had any effect on the myoclonus, but that it might sometimes be inhibited voluntarily or on the advent of paralysis in the region involved He stated that, in three-quarters of the number of cases, the causal lesions were vascular, and that the condition had sometimes occurred after epidemic encephalitis He concluded that olivary lesions were present in all cases adequately examined, and considered that the olivo-dentate system was of great importance in this condition When unilateral, myoclonus is homolateral with regard to the dentate nucleus and contralateral with regard to the olive 1173

Guillain, G (1938) *Proc R Soc Med*, **31**, 1031

OESOPHAGUS DISEASES**GENERAL MANIFESTATIONS OF OESOPHAGEAL DISEASE****Benign lesions**

Sharpe gives an account of benign lesions at the lower end of the oesophagus, and reviews the aetiology, pathology, symptomatology and treatment of cardiospasm, epiphrenal diverticula, oesophageal varices, atresia, benign ulceration of the oesophagus, stricture, benign oesophagitis and tumours, with 62 references 1176

CONGENITAL MALFORMATIONS**Imperforation****Surgical treatment**

Carter describes an operation for cure of congenital atresia of the oesophagus, the proximal segment is brought out in the neck, and the distal segment is first ligated in the mediastinum as close as possible to the communication with the trachea, is then divided, and the part of the oesophagus attached to the stomach is brought out as a 'gastrostomy tube' The advantages of the technique are (1) an ideal type of gastrostomy is provided by using the lower end of the oesophagus as a gastrostomy tube, (2) the distance between the two oesophageal stomas is so small that they could be easily joined by a skin tube The author reports a case in which simple ligation of the oesophagus with silk did not result in leakage but the patient died after 62 days from pneumonia which did not appear to be a complication attributable to the operation 1177

The surgical treatment of congenital atresia of the oesophagus has not been satisfactory but new methods devised have had some success, especially that described by Haight and Towsley The case described by them represented a direct attack on the oesophagus so that the continuity of the organ was restored A one-stage extrapleural exposure was made, with ligation of the tracheo-oesophageal fistula and simultaneous anastomosis of the two oesophageal segments The advantage of this procedure is that patients who survive are able to swallow normally In the case mentioned the operation was a success, 17 months after operation the child was well but there was some occasional regurgitation of food, X-ray examination showed a stenosis at the site of the anastomosis The child was in good general condition and had been enjoying normal activities, the weight was 23 pounds

INJURIES**Perforation by bougie**

Touffo records an unusual case of accidental perforation of the cervical part of the oesophagus, made by the flexible gastroscope, the rubber bougie became detached and remained in the oesophagus after the gastroscope was withdrawn The condition was diagnosed as instrumental perforation and was confirmed radiologically The bougie was removed through an external incision, and the perforation was repaired The patient made a complete and uneventful recovery 1179

SPONTANEOUS RUPTURE

- 1180 Mallam, Whitelocke and Robb-Smith record a case and state that 40 cases only have been published since the condition was first described by Boerhaave in 1724. In this particular case the patient was 44 years old, and was suddenly struck down by extreme pain which was not controlled by large doses of morphine. The pain was most severe in the lower thoracic region posteriorly, the abdomen was distended and rigid, and thirst was extreme. At laparotomy there was some free fluid in the abdomen, but the cause was not found until the necropsy. Diagnosis of this condition has been made once only, and therapy has never been successful, all the recorded cases having proved fatal in 12-48 hours after the onset of the symptoms.

Sequelae

Shortening

It is generally agreed that the congenital short oesophagus is rare and is not likely to be an important factor in the aetiology of chronic oesophageal ulcer. In seven cases of acquired shortening, quoted in an Annotation in the *Lancet*, all patients gave a history of chronic ulceration, the average age being 64 years. Contraction of the scar tissue drags the lax cardia through the hiatus.

ULCERATION PEPTIC ULCER OF THE OESOPHAGUS

Aetiology

- 1183 Chamberlin, discussing the aetiology of peptic ulcer of the oesophagus, suggested that, in addition to the presence of aberrant gastric mucosa which has been pointed out by many authors, a short oesophagus and a diaphragmatic hernia are also important factors. Because of the confusion existing in the literature concerning the diagnosis of the condition, he suggests the following diagnostic criteria. The ulcer must be unassociated with systemic disease, since the presence of such an ulcer is more likely to be a result of the disease than a separate entity, the ulcer must be seen at oesophagoscopy or autopsy, free gastric hydrochloric acid must be present, the ulcer must be chronic, and the symptoms must be relieved by peptic ulcer therapy and dilatation.

FUNCTIONAL DISORDERS

Non-malignant stricture

- 1185 Vinson stated that the occurrence of benign (cicatricial) stricture of the oesophagus is rarer than that of carcinoma or cardiospasm. In about 20 per cent of cases the cause is not ascertainable. In such cases carcinoma is generally suspected, and an accurate diagnosis may not be possible even on oesophagoscopical examination and microscopical examination of tissue removed. Unless the presence of carcinoma can be proved, stricture of the oesophagus should be considered as benign. Congenital shortening of the oesophagus with herniation of a portion of the stomach through the diaphragm is often associated with stricture at the junction of the oesophagus and stomach. By employing a thread as a guide for passing sounds, a benign stricture can be dilated with a minimal amount of risk and discomfort and with an excellent functional result. Complete anatomical stenosis is very rare and can be prevented by making any patient who has ingested acid or caustic swallow a thread which remains within the lumen of the oesophagus until dilatation has been effected. Gastrostomy is seldom necessary in the management of benign stricture.

Turner¹, reviewing a series of 19 cases of non-malignant oesophageal stenosis, says that, as far as could be ascertained, the causation was: corrosives, 5, congenital, 5, late results of achalasia, 4, following ulceration, 2, acute inflammation, 1, and undetermined origin, 2. He considers it highly probable that in severe illnesses, such as typhoid fever, acid and toxic stomach contents may be regurgitated into the oesophagus and cause erosion, which may not heal completely and so lead to stricture.

TUMOURS

Malignant

- 1186 Jonas states that a malignant neoplasm at or near the junction of the oesophagus and stomach, when operable, is best treated by transpleural resection and oesophago-gastrostomy, the method allows wide extirpation of the tumour and associated lymphatic structures, and later the patient can swallow normally. A procedure is described which is very similar to that which was advocated in 1940 by Carter, Stevenson and Abbott.

In cases of cervical carcinoma of the oesophagus without infection of the surrounding tissues and lymphatic glands, well planned surgical intervention holds out a much better prospect than does any other method (Turner²). Application of radium or of X-rays is not satisfactory. It is possible to remove the cervical oesophagus before a certain stage of involvement is reached, but contra-indications must be noted: (1) an advanced state of the pathological condition, (2) the age of the patient, usually over 60 years, (3) the presence of bronchitis and emphysema, (4) cardiovascular degeneration. The intrathoracic operation is to be preferred.

Annotation (1941) *Lancet*, 2, 18

OVARY DISEASES—PANCREAS, DISEASES

Vol IX
KEY NUMBERS
1186

- Carter, B N (1941) *Surg Gynec Obstet*, **73**, 485
 — Stevenson, J, and Abbott, O A (1940) *Surgery*, **8**, 587
 Chamberlin, D T (1939) *Amer J digest Dis*, **5**, 725
 Haight, C, and Towsley, H A (1943) *Surg Gynec Obstet*, **76**, 672
 Jonas, A F, Jun (1942) *Arch Surg, Chicago*, **44**, 556
 Mallam, P C, Whitelocke, H A B, and Robb-Smith, A H T
 (1940) *Brit J Surg*, **27**, 794
 Sharpe, W S (1941) *Amer J Surg NS*, **54**, 252
 Touroff, A S W (1941) *Ann Surg*, **114**, 369
 Turner, G G (1939)¹ *Brit J Surg*, **26**, 555
 — (1942)² *Proc Cardiff med Soc*, p 5
 Vinson, P P (1939) *J Amer med Ass*, **113**, 2128

OVARY DISEASES

TUMOURS

Aetiology and classification

Meigs's syndrome

In 1939 Meigs reported on 15 cases in which there was hydrothorax associated with fibroma of the ovary, the condition is now known as Meigs's syndrome. Women in the early fifties are especially affected. The diagnosis may be wrong as the disease commonly resembles peritoneal tuberculosis. After the fibroma or fibromas have been removed there is usually spontaneous and permanent disappearance of the hydrothorax.

1196

Meigs, J V (1939) *Ann Surg*, **110**, 731

OXYCEPHALY

AETIOLOGY AND PATHOGENESIS

Burkens, La Chapelle and Groen published the pedigrees of 2 cases of oxycephaly, from which it was concluded that the disease is due to a mutation transmitted as a sex-linked dominant. They rejected the hypotheses of Maria-Sainton (disturbance of ossification of membrane) and of Jansen (intra-uterine disturbance due to the pressure of a tight amniotic band), and regarded the condition as a disorder of the genes.

1198

Schwarzweiller considered that the condition was a hereditary malformation for the following reasons: (1) The existence of transmitted cases, (2) the appearance of certain isolated symptoms in other members of the family, (3) the frequent association of this and other malformations due to arrested development. He suggested that affected females should be sterilized.

In describing a case which was relieved by operation King states that it is assumed that oxycephaly is due to premature closure and obliteration of the cranial suture lines, and that blindness is probably due to increased intracranial pressure. King's operation was devised to make a mosaic of the bones of the cranial vault by making grooves to connect a series of burr-holes, and thus permit symmetrical expansion of the skull. In his case oxycephaly was associated with extreme exophthalmos, increased intracranial pressure and failing vision. The ophthalmic disks were pale and the patient was apathetic. After operation the vision improved, the exophthalmos receded greatly, the ophthalmic disks became less pale, and an appearance of alertness developed. The skull bones united.

Burkens, J C J, La Chapelle, E H, and Groen, J (1936) *Ned Tijdschr Geneesk*, **80**, 5547

King, J E J (1938) *Arch Neurol Psychiat, Chicago*, **40**, 1205

Schwarzweiller, F (1937) *Z KonstLehre*, **20**, 341

PANCREAS, DISEASES

INFLAMMATORY CONDITIONS

Pancreatitis

Acute

Diagnosis—McCorkle and Goldman record that the serum amylase test is of diagnostic value in acute pancreatitis, the serum showing marked elevation in the amylase level, a moderate increase above the normal level occurring in the early stage of acute painful abdominal disorders is diagnostic of acute pancreatitis. In certain cases parotitis and renal disease will also result in a slightly increased serum amylase level, but renal disease can be differentiated by the investigation of the urinary amylase level.

1204

Treatment—There has been a tendency in continental clinics not to operate for this condition, but to treat the patient medically. This change in opinion has also received support in America, and Pratt of Boston maintains that the disease is not an infection but an intoxication by the pancreatic ferments. He reports that at the Boston City Hospital conservative treatment reduced the mortality from 54 to 25 per cent. Elman also advocates conservative treatment at the onset of acute pancreatitis.

1204

because the symptoms may subside promptly, later, cholecystectomy may be advisable. If the acute symptoms do not subside and necrosis of the pancreas supervenes, surgical drainage of the lesser peritoneal cavity may be required. The author states that the disease is rarely fatal, and the common occurrence is generally overlooked because a clinical diagnosis can seldom be made without a serum amylase test.

TUMOURS

1208

Tumours of the islands of Langerhans

Campbell, Graham and Robinson report on 5 cases of tumour derived from the islet cells in which a tumour was removed, 3 of the patients were cured, one died after the operation, and the remaining patient still showed mental confusion and muscular incoordination after operation. The tumours all showed a high insulin content.

Carcinoma of pancreas

Levy and Lichtman report on 19 cases of primary carcinoma of the pancreas. By far the commonest symptom was pain which was present in 90 per cent of cases, it is often nocturnal and is not related to food but may be relieved by changes in posture. It may radiate to the right or left round the costal margin to the back. Generally there is considerable loss of weight, and an abdominal tumour is palpable in 50 per cent of cases. The liver and spleen may also be enlarged, but widespread metastases are uncommon. There is often disturbance of carbohydrate metabolism, and glycosuria, when it occurs, cannot be controlled easily either by insulin or by diet. Venous thrombosis is not uncommon and may be due to the pressure of the tumour on the inferior vena cava. Surgery can be palliative only but a cholecystoenterostomy often gives much relief and causes the jaundice to clear up for a time.

Campbell, W. R., Graham, R. R., Robinson, W. L. (1939) *Amer J med Sci*, 198, 445

Elman, R. (1942) *J Amer med Ass*, 118, 1265

Levy, H., and Lichtman, S. S. (1940) *Arch intern Med*, 65, 607

McCorkle, H., and Goldman, L. (1942) *Surg Gynec Obstet*, 74, 439

Pratt, J. H. (1940) *New Engl J Med*, 222, 47

PARAPSORIASIS

DIFFERENTIAL DIAGNOSIS

1213

From mycosis fungoides

Much attention has been given to cases of parapsoriasis in which mycosis fungoides tumours develop, and the general trend of opinion in Great Britain and in America is to regard them as mycosis fungoides in spite of the frequent absence of itching and failure to respond to X-ray therapy.

PARATHYROID GLAND DISEASES

HYPERPARATHYROIDISM

Clinical types

Werner's syndrome

1216

In 1934 Oppenheimer and Kugel recorded cases of a syndrome they termed Werner's syndrome, and some years later reported the changes found at necropsy. The syndrome is a heredo-familial disorder with premature baldness or greyness, sclero-poikiloderma, premature cataracts, shortness and slenderness of stature, with associated juvenile characteristics suggesting arrested development, hypogonadism and premature senescence resembling that seen in progeria. Blue sclerotics were seen in 2 of the authors' 3 cases, osteoporosis and metastatic calcification were present in each case. In one case 2 slightly enlarged parathyroid glands were found at necropsy. The authors consider that the disease is associated with hyperparathyroidism rather than with a pluriglandular disturbance.

Oppenheimer, B. S., and Kugel, V. H. (1934) *Trans Ass Amer Phys*, 49, 358

— (1941) *Amer J med Sci*, 202, 629

PAROTID GLAND DISEASES

PNEUMOCOCCAL PAROTITIS

1217

Payne¹ reports on a case of acute suppurative pneumococcal parotitis in which, a few months after the parotitis, the auriculo-temporal syndrome developed. This rare condition is characterized by hyperaemia and sweating in the area supplied by the auriculo-temporal nerve, and to a lesser extent in the area supplied by the third division of the fifth nerve and by the great auricular nerve. These symptoms are evoked by eating and are initiated by a taste reflex from the posterior third of the tongue. In some cases there are also tingling and pain, and some patients have shown sensory disturbances in the affected area. The condition is usually persistent, although complete recovery has been reported. In the case described the symptoms have lasted for 30 years.

Payne² describes pneumococcal parotitis as a clinical entity possessing many

characteristic features. The disease may occur in an acute, recurrent or chronic form. The recurrent cases form the largest group, and in this type the exacerbations tend to be more acute and more severe than those in cases of parotitis due to *Streptococcus viridans*, at times such exacerbations pass unexpectedly to suppuration within the gland and cause notable constitutional disturbance. In recurrent cases the parotid saliva is characteristically profuse and tenacious and contains pus and a large quantity of mucus. Recurrent cases may begin during infancy, during the period of the second dentition, or during the first half of adult life, they tend to be more common in females. Suppuration and fistula formation are the only probable complications. In the acute group fulminating cases do not occur. In all types the prognosis, as regards life, is good.

Payne, R. T. (1940)¹ *Lancet*, 1, 634

— (1940)² *Brit med J*, 1, 287

PATERNITY, DISPUTED

BLOOD GROUPS AS EVIDENCE OF NON-PATERNITY

1227

A Bill was introduced in the House of Lords during the Session 1938-9 to enable blood tests to be demanded by a party or ordered by the court in bastardy cases. Preoccupation with emergency measures on the outbreak of war caused the Bill to be dropped, but the Report of the Select Committee of the House of Lords on the Bill (H. L. Paper 173) is of interest.

The Select Committee were unanimously of opinion that the qualities of blood underlying blood grouping, and the laws of inheritance governing the transmission of these qualities from parents to children, were accepted by such a consensus of scientific opinion throughout the civilized world as to render it desirable in the interests of justice for this knowledge to be applicable to affiliation cases. They were much impressed by the unanimously favourable testimony of the eminent pathologists who appeared before them. There was a preponderance of medical and legal opinion in favour of the use of blood tests as evidence in affiliation cases.

The Committee throughout recognized that it was not yet possible to determine scientifically that a particular man was the father of a particular child and that the tests established negative and not positive conclusions. It was also accepted that in only one case in three, where an innocent man is concerned, could paternity be absolutely excluded by the tests. The Committee were satisfied that the risk of error in the making of blood tests had been reduced to negligible proportions and that the tests not only might, but would, prevent injustice. In those cases in which the tests exclude paternity the public were becoming ready to accept the positive verdict of science when it declared that the man could not be the father of a particular child.

Detailed recommendations were made of which the following are relevant to the present work.

(1) No difficulty should be found in obtaining a sufficient and suitable sample of blood from a young baby, as the sample would be taken by experienced persons, if the blood were taken from the heel a sufficient sample was easily obtained.

(2) Several questions arose as to the best way of dealing with the blood samples when taken.

(a) Should they be treated with sodium citrate or oxalate, or forwarded undiluted to the testing centre? The view of the majority of pathologists who gave evidence was that it is better to forward whole blood untreated, as being both surer and simpler, and this view the Committee have adopted.

(b) How to avoid error in identifying the sample with the person or child from whom it was taken? Two systems in use today were demonstrated, in which differently coloured test-tubes were used to distinguish the samples taken from the man, woman and child, these were enclosed in a strong wooden container. The Committee were satisfied that if a standardized system on these lines were employed, the risks of error and of damage in transit would be negligible.

(c) How should the blood sample taken by the appropriate medical practitioner be forwarded to the approved testing centre? The evidence showed that untreated blood samples would keep in good condition for testing purposes for approximately 48 hours. The Committee decided that in the vast majority of cases the ordinary post would convey samples to their destinations well under the specified time.

(3) As regards the question of identification of parties to avoid the possibility of substitution or impersonation, it appeared to the Committee that although the confrontation would be impossible in many instances where the parties were residing in different parts of the country, the child and its mother should always be required to appear together to undergo the test.

Harley and Lynch, in presenting the results of blood-group tests in 50 cases of disputed paternity, emphasize the point that the test may establish the innocence of a man accused of paternity, but can never prove that he is the father. Of the 50 cases, in 8 non-paternity was established and in 42 non-paternity was not estab-

1227

lished The result in the 8 established cases was based in 3 cases on the ABO system of agglutinogens, in 4 on the MN system and in one on both systems Harley, D., and Lynch, G. R. (1940) *Lancet*, 1, 911

PEMPHIGUS AND PEMPHIGOIDS

PEMPHIGUS VULGARIS

Definition

1230

The history of pemphigus has been reviewed, starting with the era of Hippocrates and ending with present-day data (Lever and Talbott) Pemphigus vulgaris, originally described by Wichmann in 1791, was classified by Hebra under this title and it has been referred to ever since as pemphigus vulgaris In 1844 Cazenave described pemphigus foliaceus and in 1886 Neumann described pemphigus vegetans The malignant acute pemphigus of Brocq is of comparatively recent distinction, but two other and less known types are (1) the pemphigus of mucous membranes described by Thost and by Serefis and (2) the pemphigus erythematodes which has many of the characteristics of lupus erythematosus

Lever, W. F., and Talbott, J. H. (1942) *Arch. Derm. Syph., N.Y.*, 46, 800

PEPTIC ULCER

PEPTIC ULCER OF STOMACH AND DUODENUM

Course and prognosis

Peptic ulcer in the forces

1236

Breakdown during service with the Forces on account of peptic ulcer has been shown in most cases to be due to the recurrence of an old ulcer and not to the formation of a fresh ulcer Allison and Thomas reported radiological evidence of peptic ulcer in 45 of 100 dyspeptic sailors examined Graham and Kerr found 55 per cent of 246 cases of digestive disorder in soldiers to be associated with duodenal ulcer and 9 per cent with gastric ulcer Peptic ulcer constitutes a major cause of sickness among our Forces Payne and Newman had previously noted that peptic ulcer was the cause of digestive trouble in 78 per cent of proved cases out of 287 soldiers investigated The official decision regarding ulcer is to discharge all men with proved ulcer

Treatment

Cure of ulcer

Medical treatment—Alstead studied the effects of giving bismuth carbonate to healthy and to ulcer subjects Therapeutic doses had very little effect upon gastric acidity The drug showed little tendency to line either the gastric mucosa or an ulcer crater, and Alstead concludes that it has little value as either an antacid or an astringent for the stomach When its pain-relieving properties were compared with those of lactose or dried milk—the patient being unaware of the altered therapy—there was not any appreciable difference to be found

Nicol studied the results of treatment in 387 patients on discharge from hospital and at periods of between 2 and 12 years after discharge, with an average of 4 years He found that approximately three-quarters of the number of patients, whether they were treated medically or surgically, were free from symptoms on discharge, but after from 2 to 12 years less than one-fifth (16.8 per cent) had remained free Forty-one per cent had been well enough to work if they were careful with their diet The best results appeared to follow the operation of gastro-enterostomy for organic pyloric stenosis (82 per cent were symptom-free or were improved) The results of treatment for gastric ulcer were worse than those for duodenal ulcer, but the exact form of treatment employed (whether medical or surgical) or the duration of symptoms before admission to hospital had little influence on the end-results or on the number of relapses

Several further reports have emphasized the good results of fuller diets in the treatment of peptic ulcer, as compared with the older types of progressive fluid diets, especially in the treatment of bleeding ulcers Thus Eichhorn found that of 43 patients with bleeding peptic ulcers treated by initial starvation, the mortality was 19 per cent, and of 38 who were treated by immediate feeding as advocated by Meulengracht in 1932, there were not any deaths

In cases of chronic gastric ulcer certain claims have been made that vitamin A has a beneficial effect on patients but Douthwaite has disproved this In cases of chronic gastric ulcer the patients were allowed to eat ordinary food and to take the usual amount of exercise without having any extra rest The diagnosis of chronic gastric ulcer had been confirmed by X-ray examination and by the presence of occult blood in the stools So far from being benefited by having 120,000 units of vitamin A every day for 21 days, 8 patients actually became worse and at the end of the course of treatment the size of the ulcer was not less Furthermore, after ordinary medical treatment was resorted to all these patients showed improvement The same results

were noted in 3 patients who were given double the dose of vitamin A for 4 weeks. The greatest surprise was caused by one patient who was allowed to smoke as much as he wished during the treatment and who was given 120,000 units of vitamin A daily for 14 days, at the end of this period he did not have any pain and on X-ray examination there was not any visible ulcer.

Surgical treatment—A review of the surgery of peptic ulcer in 1940 showed that the mortality for partial gastrectomy for duodenal ulcer was 3.9 per cent, and for gastro-enterostomy 1 per cent. The former operation was performed four times more often than it was in 1936, owing to better selection of cases. The proportion of duodenal to gastric ulcer cases was approximately 15:1, and over 50 per cent of the gastric ulcer patients attending the clinic were submitted to operation, this was partly because approximately 10 per cent of lesions which were diagnosed as gastric ulcer proved at operation to be malignant. The mortality rate of operations for anastomotic ulcer was 6.2 per cent (Gray, Walters and Priestley).

One thousand operations on the stomach and duodenum were done at the Mayo Clinic in 1941, with a mortality rate of 4.3 per cent. There were 435 persons suffering from duodenal ulcer and of these 80 per cent were operated on. In the 215 cases of resection the mortality was 2.8 per cent and of 198 patients with conditions in which gastro-enterostomy was carried out there was a mortality of 1.5 per cent. Surgical treatment was the last resort. There were 97 cases of gastric ulcer, in 88 of which partial gastrectomy was done, and 1.1 per cent proved fatal. Of 27 patients who had both conditions and upon whom gastrectomy was performed, there were not any deaths (Walters, Gray, Priestley and Counsellor). Partial gastrectomy is therefore safe and it is recommended in chronic gastric ulcer. The total mortality of patients upon whom partial gastrectomy for non-malignant lesion was performed was 2–6 per cent.

Treatment of complications

Haematemesis—Research on the changes in volume and haemoglobin of the blood and other blood chemical investigations in cases of severe gastric haemorrhage showed that blood transfusion was a most important factor in saving life, together with avoidance of dehydration and provision of sufficient food intake. Out of 143 cases of gastro-duodenal haemorrhage, 18 patients died. Except in a few cases operation was delayed until the bleeding had stopped and time had been allowed for the patient to recover from the anaemia. There was not any evidence that the transfusion of blood made haemorrhage more likely (by raising blood pressure) and the authors regard a blood haemoglobin of 40 per cent as the level at which further bleeding is likely to prove fatal, and as calling for transfusion. Of 40 patients who were given transfusions, the average amount of blood was 1,500 cubic centimetres, at the rate of 1 pint in from 4 to 5 hours (30–40 drops per minute) (Bennett, Dow and Wright).

Allison, R. S., and Thomas, A. R. (1941) *Lancet*, 1, 565

Alstead, S. (1941) *Lancet*, 2, 420

Bennett, T. I., Dow, J., and Wright, S. (1942) *Lancet*, 1, 551

Douthwaite, A. H. (1942) *Guy's Hosp. Rep.*, 91, 97

Eichhorn, J. P. (1942) *Amer. J. med. Sci.*, 203, 428

Graham, J. G., and Kerr, J. D. O. (1941) *Brit. med. J.*, 1, 473

Gray, H. K., Walters, W., and Priestley, J. T. (1941) *Proc. Mayo Clin.*, 16, 721

Nicol, B. M. (1942) *Lancet*, 1, 466

Payne, R., and Newman, C. (1940) *Brit. med. J.*, 2, 819

Walters, W., Gray, H. K., Priestley, J. T., and Counsellor, V. S. (1942) *Proc. Mayo Clin.*, 17, 420

PERITONITIS: I.—ACUTE PERITONITIS

Addenda

In Vol. IX, p. 543, line 4, add the sentence: When contamination of the peritoneum is probable, as in some operations on the colon, prophylactic administration of sulphanilamide is advisable.

On p. 543, at end of second paragraph under *Removal of pus*, add: In severe peritonitis it may be wise to apply sulphanilamide to the infected area. After the pus has been evacuated the powdered drug may be insufflated into the dried infected surface. Since it has been shown that sulphanilamide has a direct local deterrent effect on the streptococcus, this should be sufficient justification for its local application, but, in addition, absorption into the general circulation takes place and some have recommended its administration by this method and that later its supply should be maintained by oral or parenteral administration.

On p. 544, after last line on page, add: Sulphanilamide has a powerful effect on the gonococcus and should be administered in gonococcal peritonitis. In cases of pneumococcal peritonitis it is better to use sulphydrydine which has a greater effect on the pneumococcus (Lockwood and Rhoads, Ravdin, Rhoads and Lockwood).

TREATMENT

- 1241 Several authors have recommended drugs of the sulphanilamide group in the treatment of peritonitis, and Corry, Brewer and Nicol have proved their value. In several of their patients anaerobic and actinomycotic organisms were present in the peritoneal cavity, the value of these drugs in preventing the late development of actinomycosis after appendicular perforating peritonitis is therefore obvious. Corry, Brewer and Nicol concluded that soluseptasine and proseptasine caused fewer toxic symptoms than did sulphanilamide, although by some observers the former drugs are not considered to be so efficacious.
- The dosage was as follows: Soluseptasine 0.5 gramme 4-hourly, that is, 3 doses given either intramuscularly or intravenously in saline, 0.5 gramme 6-hourly as above or by rectum or mouth. As soon as the patient is doing well a change should be made to proseptasine 1 gramme 3 times a day by mouth until the temperature remains normal for 24 hours. Sulphanilamide. In the operating theatre 10 cubic centimetres of a 5 per cent solution (0.5 gramme) is administered intramuscularly. First hour 2 tablets (each 0.5 gramme) in 10 ounces saline rectally, 2nd hour 10 cubic centimetres intramuscularly, 4th hour 1 tablet by mouth, 7th hour 2 tablets rectally in saline, 11th hour 2 tablets by mouth, 13th hour 1 tablet rectally in saline, 15th hour 1 tablet by mouth, 19th and 23rd hours 1 tablet by mouth, second, third and fourth days 2 tablets (1 gramme) by mouth 3 times a day, on the fifth, sixth and seventh days 1 tablet (0.5 gramme) by mouth 3 times a day.

Corry, D. C., Brewer, A. C., and Nicol, C. (1939) *Brit med J*, 2, 561
Lockwood, J. S., and Rhoads, J. E. (1939) *Surg Clin N Amer*, 19, 1457

Ravdin I. S., Rhoads, J. E., and Lockwood, J. S. (1940) *Ann Surg*, 111, 53

PINK DISEASE

TREATMENT

- 1261 Good results have been reported from the use of vitamin B₁₂ given orally or intramuscularly. By mouth the dose suggested is 600 units daily and by the intramuscular route 2,000 units every other day.

PINTA

CLINICAL PICTURE

Cuban form

- 1262 Saenz, Triana and Armenteros describe the special clinical features of pinta in Cuba. In its primary stage the disease is limited exclusively to the palms and soles, with subsequent extension to the backs of the hands and in some cases to the arms and legs. An outstanding characteristic of the Cuban cases also is keratosis of the palms and soles. The first manifestation of this consists of rounded or irregularly outlined hyperpigmented spots which enlarge peripherally, at the same time becoming more numerous. The skin appears dry and yellowish and becomes squamous at times when involvement is severe. In rare cases it also shows the sago-like hardened claviform keratosis. In a more advanced stage the pigment disappears, with resulting production of permanent achromic areas. The colour of the pigmentary disturbances is always slate blue. In some cases there are hard multiple non-inflammatory medium-sized superficial enlargements of the lymph nodes. In a few cases there is thickening with partial or total black pigmentation of the nails.

Saenz, B., Triana, J. G., and Armenteros, J. A. (1940) *Arch Derm Syph*, N. Y., 41, 463

PLAGUE

Corrigendum

In Vol IX, on pp 683 and 684, *Ceratophyllus fasciatus* is given as the name of the chief European rat-flea. This name was strictly already obsolete (Jordan), and the new generic name *Nosopsyllus* for this species group has become current in medical literature. *Ceratophyllus fasciatus* and *C. fasciatus* should therefore read *Nosopsyllus (Ceratophyllus) fasciatus* and *N. fasciatus*.

EPIDEMIOLOGY

Geographical distribution

Present-day statistics

- 1276 For a decade the incidence of human plague has been everywhere on the wane. Only 17,002 deaths were recorded in all India during 1936 as against 1,328,249 in British India during the plague year of 1904-5 when the pandemic was at its height. Nevertheless, although plague among domestic rats and man has diminished so much during recent years, the infection is still slowly but continuously spreading among a great variety of species of field rodents, including the gerbilles of the South African veldt, the cavies of the South American pampas and the ground squirrels of the mountains and prairies of the Western United States of America. There are links between these rodents of the plains and urban rats at the margin of cultivation, thus one effect of the present pandemic has been to extend the territories subject to

enzootic plague and to multiply the possible sources of future epidemics. Formerly the Asiatic marmots constituted the sole permanent reservoir of infection from which the pandemics of the past arose. Accordingly recent research has been increasingly concentrated on the complicated oecology of field rodent plague. The work of Eskey and Haas on wild rodent plague in the Western United States of America is a good example of this trend. Eskey's earlier studies were on the effect of local variations in the numerical prevalence of *Xenopsylla cheopis* and other species of rat-fleas on the spread of plague in Ecuador, Peru and the Hawaiian Islands. These American researches supplement previous work on similar lines by British observers in India, Ceylon and Central Africa. Systematic surveys on rodents and rodent fleas have proved to be an indispensable guide to preventive measures against plague and go far to explain the relative immunity from plague of some areas and the severity of epidemics in others.

PROPHYLAXIS AND TREATMENT

General prophylaxis

Antiplague vaccines

The prophylactic value of antiplague vaccines made of living avirulent strains of *Pasteurella pestis* of high immunogenic power is now established. Millions of people have been inoculated with such vaccines in Java and Madagascar without accident and with a greater reduction of plague incidence than that which results from the inoculation of killed vaccines of the Haffkine type. In the early days of the apparently irresistible progress of plague in India the authorities were inclined to adopt a fatalistic attitude towards measures designed to control the spread of infection. After the failure of time-honoured procedures based on faulty epidemiological conceptions, reliance was placed on mass inoculation with the Haffkine vaccine and the mass evacuation of villages. Recent research has provided better weapons against plague and good results now reward a more active policy. The results of rat-flea surveys often enable the real danger zones to be marked out and the available antiplague resources to be concentrated on them. Both man and the domestic rat subsist mainly on cereals, and the principal plague flea, *X. cheopis*, breeds most freely in the debris of grain. Hence the rat-proofing of granaries, markets and food-stores is the best permanent safeguard and destruction of rats by modern methods is the best interim plague preventive measure. Heavily infected localities in India have been freed from plague by the repeated fumigation of rat burrows with hydrogen cyanide gas and in South America by the laying of millions of effective poison baits. Unfortunately all export granaries are not efficiently rat-proofed. If there is reason to suspect that such premises are the scene of epizootics, then the produce, when it reaches its destination, should be fumigated, especially when the climatic conditions favour the transfer of infected rat-fleas. Thus Ceylon was not finally freed from plague until rice imports were systematically fumigated in Colombo harbour with cyanide gas.

Medical treatment

Specific therapy

Specific therapy for plague has followed three main lines of development—those of serum therapy, chemotherapy and bacteriophage therapy. Although confident claims have been made for bacteriophage therapy, its value is very dubious. Harvey has reviewed the literature. During a long period serum therapy proved to be disappointing for the treatment of the highly lethal Indian bubonic plague, recently, however, better results have been obtained with more potent serums, on the other hand notable reduction of mortality occurred after treatment with antiplague horse serum in South America, New Orleans and Australia, where bubonic plague tends to be less virulent. Lloyd recommended the early use of large and repeated doses of freshly prepared serum given intravenously. He treated 1,491 patients who had bubonic plague at Guayaquil and the mortality was reduced from 60 per cent to 33 per cent.

Chemotherapy

A considerable amount of literature on the treatment of plague with the sulphonamides has now accumulated, and good results in bubonic cases are reported from India, Madagascar, Egypt, Peru, Central Africa, Spain and Argentina. Animal experiments and clinical trials both indicate that sulphathiazole is the best drug of the group to use. Sokhey and Wagle recommend doses totalling 10 grammes for the first day, 7.5 grammes for the next 4 or 5 days and smaller doses later to maintain an effective therapeutic concentration in the blood (5–10 milligrams per 100 cubic centimetres). They conclude from their controlled comparative tests that the efficacy of sulphathiazole is evident and may be enhanced when combined with serum treatment. Fleming reports that the plague bacillus is resistant to penicillin. Pneumonic plague fails to respond to any treatment.

Eskey, C. R., and Haas, V. H. (1940) *United States Public Health Bulletin*, No 254.

Fleming, A. (1944) *Brit med Bull*, 2, 4.

Harvey, W F (1933) *Trop Dis Bull*, **30**, 331, 411
Jordan, K (1933) *Novitates Zoologicae*, **39**, 70
Lloyd, B J (1925) *J Amer med Ass*, **85**, 729
Sokhey, S S, and Wagle, P M (1943) *Rep Haffkine Inst*, Bombay

PNEUMONIA, LOBAR

AETIOLOGY AND BACTERIOLOGY

Types of pneumococci

Association of type and lesion

- 1279 Of 200 cases investigated by Meakins and McKenna the type of pneumococcus responsible was type I in 30 cases, with 3 deaths, type II in 39 cases, with one death, type III in 39 cases, with 9 deaths, type IV in 12 cases, with one death, type V in 19 cases, with one death, type VI in 8 cases, with one death, type VII in 18 cases, with 2 deaths, type XI in 6 cases, with 2 deaths, type XIV in 3 cases, with one death, in the remaining 26 cases XII, XVII, XVIII, XIX, XX, XXIII, XXIV and XXVII were responsible and there was not any associated mortality

PATHOGENESIS AND MORBID ANATOMY

Pathogenesis

Mode of origin of pneumonia

The summary by Robertson of the various means of access to the lung by pneumonia organisms is very useful. Droplet inhalation or the presence of fluids in the larynx may allow organisms to gain access to the lung. Infection from the air is not common, animal experiments in which attempts were made to produce infection by exposure to atmospheres containing infected droplets were unsuccessful. It is obvious that infective material inhaled deeply from the upper respiratory passages is one of the main factors in infection. Liquids pass the ciliary barrier much more easily than do solids, again animal experiments have proved that this is the case. The epiglottis may not be the ideal closed door against infection; there may be an aperture and cold is one of the factors which lead to imperfect closure. Robertson produced lobar pneumonia in dogs by first lowering the body temperature by from 3–5° F and then injecting a suspension of pneumococci and starch into a terminal bronchus. Irritation has also to be considered as a major factor in the pathogenesis of pneumonia, animals given a non-irritative suspension of pneumococci were unaffected unless large amounts of pneumococci were used. The above explains pneumonia as a sequel of general anaesthesia and especially in patients in whom there is infection of the upper respiratory passages.

COURSE AND PROGNOSIS

Factors influencing prognosis

Type of pneumococcus

According to Meakins and McKenna, who made an analysis of a series of 200 cases of pneumococcal lobar pneumonia, certain types of infection predispose to a fatal ending. There were 21 fatal cases in the series, these giving a mortality rate of 10.5 per cent. Sex had apparently no bearing on the mortality rate although the incidence was three times as great in males as in females. In every fatal case the age of the patient was over 40 years, infants excepted, the average age of the patients who died was just over 56 years whereas the average age of those who survived was 36 years. A type III infection is apparently a most dangerous one, since 23.5 per cent of those affected in this way succumbed. Bacteraemia was very common in all fatal cases, and it is notable that over 90 per cent of the patients who died had other diseases affecting the circulatory, pulmonary, renal or hepatic systems. Meakins and McKenna suggest that the recognition of non-specific factors not only from the point of view of the prognosis, but also on account of the treatment, would decrease the number of deaths.

TREATMENT

Non-specific treatment

Sulphonamide compounds

Since the introduction of the sulphonamide compounds in the treatment of pneumonia a vast amount of literature has accumulated and many reports have been made. In summing up the situation the number of substances available and their terminological handicaps must be kept in mind. Sulphapyridine, which made a name for itself in the form of M & B 693 in 1938, has become established as a substance of reliability in most cases of pneumonia. As a rule the initial dose for an adult is 4 tablets of a $\frac{1}{2}$ -gramme each and 1 gramme 4-hourly until the temperature becomes normal and remains so for 48 hours. Thus in an ordinary case of pneumonia the amount of sulphapyridine given would be about 20 grammes spread over 4 days. Two main disadvantages are well known. The first is that idiosyncrasy occurs in a certain number of patients, the reactions being vomiting, cyanosis and dermal eruptions. Occasionally the addition of an alkali may stop the vomiting, but sometimes the administration of sulphapyridine itself may have to be discontinued. The

occurrence of cyanosis, the result of methaemoglobinaemia, is apt to convey the idea that the disease is worse than it actually is. There are various methods of counteracting the condition, but none has yet been established as infallible. It is now known that sulphaemoglobinaemia does not occur when the sulphonamide group of drugs is used in pneumonia, and therefore eggs and similar sulphur-containing articles of food may be ordered for the patient. One of the greatest dangers is that of agranulocytosis, and unless the sulphonamide is stopped at once there is a risk of fatal termination. The second disadvantage is that sulphapyridine, although it has undoubtedly reduced the death rate in pneumonia in patients under 40 years of age, has not been equally successful in those above this age. Thus the death rate from pneumonia is still considerable in the latter category. With regard to sulphathiazole, there is less likelihood of toxic effect and greater scope in treatment, the drug is not so powerful as is sulphapyridine and the patient requires about 30 grammes spread over 4 or 5 days. So far as sulphadiazine is concerned the use of this substance has had success in conditions caused by pneumococci, staphylococci and the Friedlander bacillus. Sulphadiazine does not produce toxic reactions as a rule but the drawback to this drug, and to sulphathiazole too, is that as a result of crystallization in the kidney, haematuria and anuria have resulted in certain cases. To overcome the renal disadvantages another drug, sulphamethazine, has been introduced and it seems that owing to its solubility there is less likelihood of complications occurring in the kidney. The amount required is about 30 grammes in all, an initial dose of 4 grammes being given and 1 gramme 4-hourly afterwards for about 4 days. According to Macartney, Luxton, Smith and Ramsay, sulphamethazine has a high degree of therapeutic efficiency and it tends to reduce to the minimum the complications referred to above. Maxwell points out that in the case of sulphapyridine treatment drug fever occasionally occurs as a complication. Here the temperature rises or at least remains stationary, despite the usual dose of the sulphonamide drug. It is advisable to discontinue the use of the drug if the patient is still in a state of hyperpyrexia after 48 hours of treatment.

The investigations of Stahle confirm the findings referred to above, and as they cover no less than 15,000 cases of pneumonia among people with small incomes they are of the utmost importance. The majority of the patients were treated with sulphapyridine or sulphathiazole and sometimes serum therapy was also used, the latter, however, is best employed when the response to chemotherapy is poor. Stahle stresses that chemotherapy if properly conducted gives rise to very few severe toxic reactions and the earlier the treatment is given the better.

Medicinal and symptomatic

Administration of oxygen

There have been great developments in the methods of administering oxygen, notably by the use of the B.L.B. mask introduced by Boothby, Lovelace, and Bulbulian. This consists of a mask with a rubber bag and various adjustments, by which an alveolar concentration of oxygen of more than 40 per cent can be maintained with a flow of 3 litres a minute, a concentration of from 55 to 60 per cent with a flow of 4 litres, and from 90 to 95 per cent or even 100 per cent with a flow of from 6 to 8 litres (Boothby, Lovelace, Bulbulian).

The Tudor Edwards spectacle-frame nasal catheter carrier with a flow-meter and humidifier is also of value. It is probable that the former method of administration will very largely supplant the oxygen tent except for very sensitive patients, for surgical operations on the chest, and for infants and children.

Boothby, W. M. (1938) *Proc Mayo Clin*, 13, 641

Bulbulian, A. H. (1938) *Proc Mayo Clin*, 13, 654

Lovelace, W. R. (1938) *Proc Mayo Clin*, 13, 646

Macartney, D. W., Luxton, R. W., Smith, G. S., and Ramsay, W. A. (1942) *Lancet*, 1, 639

Maxwell, J. (1943) *Practitioner*, 151, 204

Meakins, J. C., and McKenna, R. D. (1943) *Canad med Ass J*, 48, 104

Robertson, O. H. (1943) *Ann intern Med*, 18, 1

Stahle, D. C. (1942) *J Amer med Ass*, 118, 440

PNEUMOTHORAX, SPONTANEOUS

TREATMENT

Of high-pressure type with non-healing valvular slit in lung

Chandler recommended for these cases the following simple method of treatment which was used successfully in one patient. An artificial pneumothorax refill needle of wide bore, or a small cannula, is inserted into the pleural cavity, to the proximal end of the needle is tied a thin rubber finger-cot, the closed end of which is slit. This makes a perfect valve, allowing air to escape from the pleural cavity but not to return. If the diameter of the needle or cannula is sufficiently large, any amount of air will be blown off from the pleural cavity, and the patient is at once relieved. In the case in point, a man 58 years of age, the heart returned from the mid-axillary

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line to its normal position in a few minutes, and the cyanosis and dyspnoea were proportionately relieved

Owing to cough, movements, or surgical emphysema of the chest wall, the needle or cannula is apt to be displaced very soon, the distal end gradually or suddenly working its way into the chest wall, and the valve ceasing to act. To prevent this, Chandler employed the self-retaining cannula described by Cope, and tied the finger-cot to the curved exit tube. This acted perfectly, the instrument remaining in position for 11 days without displacement. Clotted serum blocked the lumen occasionally, but this was easily dealt with by removing the inner cannula. The most meticulous aseptic and antiseptic precautions must be taken.

There are many objections to using a self-retaining rubber catheter, namely collapsibility, difficulty of cleaning if blocked, and difficulty with removal and reinsertion. The Cope self-retaining metal cannula obviates such difficulties. It might, however, be possible to use a self-retaining rubber catheter with a cannula, the latter being retained permanently in position. The catheter and cannula, however, would have to be very small, and it is doubtful if the flange of so small a catheter would be sufficiently strong to be really self-retaining.

This valve mechanism, in addition to relieving cyanosis, dyspnoea, and mediastinal displacement, promotes to a great extent re-expansion of the lung. It may succeed in closing the rent, by bringing the ruptured part of the lung up to the chest wall, where adhesions may form. This, however, may not happen, and then the moment the valve mechanism is removed, the symptoms will recur.

Recourse must therefore be had to injection of gomenol in olive oil, as described in Vol IX, p 750. If this fails to irritate the pleura, sodium morrhuate solution might be tried. The rationale of this is to set up a mild aseptic pleurisy with exudation of a small amount of highly fibrinous fluid. This clots and stimulates the process of progressive obliterative pleurisy.

Cope, Z (1939) *Brit med J*, 1, 331

POISONS LEGISLATION. MEDICAL ASPECTS

POISONS

Legislation

Vol X

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Poisons List (Amendment) Order, 1938

By this Order benzedrine and sulphanilamide are added to Part I of the Poisons List together with related substances, so that they may be supplied to members of the public only through chemists. Benzedrine is added to the Seventh Schedule and must be labelled 'Caution. It is dangerous to take this preparation except under medical supervision', instead of 'Poison', when made up ready for the internal treatment of human ailments. Benzedrine in inhalers is exempt from all control. Under sulphanilamide and its derivatives the following substances, among others, are included: colulanyde, P A B S, prontosil album, streptocide, sulphonamide-P, prontosil soluble, prontosil rubrum, proseptasine, M & B 125, rubiazol, and soluseptasine.

All these substances are added to the First Schedule of the Poisons Rules, and in addition sulphanilamide and its derivatives are added to the Fourth Schedule, and therefore may be supplied only upon the prescription of a duly qualified medical practitioner, registered dentist, or registered veterinary surgeon.

The Poisons (Amendment) Rules, 1938

These Rules render it unnecessary for a signed order for a First Schedule poison (other than a 'dangerous drug') from a duly qualified medical practitioner, registered dentist, or registered veterinary surgeon or hospital to bear the statement of the purpose for which the poison is required.

They provide also that local anaesthetics for injection in the treatment of human and animal ailments need not be supplied in fluted bottles.

Poisons List (Amendment) Order, 1940 the Poisons (Amendment) Rules, 1940

The above enactments bring within the First and Fourth Schedules of the Poisons Rules sulphapyridine and related products. The effect is that these may be supplied to the public only upon the prescription of a duly qualified medical practitioner, registered dentist, or registered veterinary surgeon. Among the substances so included in the First and Fourth Schedules are the following: albucid, ambesid, ambesid soluble, dagenan, M & B 693, methylsulphonol, rodilone, rubiazol, injectable, sulphapyridine, 2 (*p*-aminobenzenesulphonamino) pyridine, sulphonol, alkyl sulphonals, trional, and uleron.

Chloride of antimony in polishes has been removed from all restrictions, and sanogyl toothpaste has been removed from the First Schedule so that it is saleable without the purchaser's signature being required in the Poisons Register.

The Poisons (Amendment) (No 2) Rules, 1940

By these rules strychnine, which includes the salts of strychnine, may be supplied to farmers who require it for the destruction of moles, but for no other purpose, in quantities not exceeding 4 ounces avoirdupois at a time, upon a certificate in the

prescribed form issued by the County War Agricultural Committee. The certificate is retained by the supplier, to whom the purchaser must be known. The purchaser must sign the seller's poisons register.

The Poisons (Amendment) Rules, 1941

These rules permit the sale and use of strychnine for killing seals. Purchases are made only on certificates issued by 'a person duly authorized by the Secretary of State'.

The Poisons (Amendment) Rules, 1942

These rules exempt 'Surgical spirit containing not more than 0.015 per cent of brucine' from the restrictions on the sale of poisons. By the Methylated Spirits Regulations, 1930, such spirit must, however, be labelled 'For external use only—not to be taken'. It takes the place of spirit previously denatured with diethyl phthalate.

The Pharmacy and Medicines Act, 1941

This Act amends the Pharmacy and Poisons Act, 1933, in certain respects, repeals the Medicine Stamp Duties, and imposes certain restrictions upon the sale of medicines.

The amendments of the Pharmacy and Poisons Act, 1933, concern the extent to which a person who is 'an authorized seller of poisons' may sell drugs at a shop where there is not a pharmacist in charge, they also extend the powers of the Statutory Committee of the Pharmaceutical Society.

The sections dealing with medicines provide for the repeal of the Stamp Duties and for the maintenance, so far as possible, of the situation which had been brought into being by the Medicine Stamp Duties whereby formulae were disclosed on most proprietary medicines and there was a restriction to a limited class of seller of some medicines sold with recommendations about their therapeutic value. Restrictions upon the advertising of medicines are included.

The Pharmacy and Poisons Act, 1933, required an 'authorized seller of poisons' to have a pharmacist in control of any premises where he carried on a business which included the retail sale of drugs.

Section 1 of the Act of 1941 now defines the position more closely. It lays it down that it shall only be necessary for an authorized seller of poisons to have a pharmacist in control of a business where the drugs sold (including veterinary medicines and medical and surgical appliances) form a substantial part of the business. What is a substantial part of a business is left to be determined by the Courts, subject to any regulations which the Home Secretary may make.

Certain things are prohibited at shops where there is no pharmacist. These include the selling of 'loose' drugs, compounding or dispensing, the receipt of prescriptions and the distribution of medicines compounded or dispensed for the needs of a particular person, and the use of certain titles. The Act further declares that each separate department of a business is to be regarded as a separate premises. The effect is that the extent to which a business in drugs is to be regarded as substantial will be determined by reference to the business of the department and not by reference to the total business undertaken in the establishment (s. 3).

Provision is made for shops of an authorized seller of poisons, at which it is proposed to sell Part II poisons but no drugs and no Part I poisons, to be listed by a local authority (s. 2).

The functions of the Statutory Committee of the Pharmaceutical Society are enlarged by bringing within their jurisdiction cases of misconduct or of conviction for a criminal offence at a time when he was not registered, on the part of an applicant for registration as a pharmacist. The Statutory Committee is also given power to consider cases in which a corporate body is involved at a time when it is not an authorized seller of poisons (s. 5).

In both cases the Committee may direct that the registration of the individual or the qualification of the corporate body as an authorized seller of poisons shall be suspended.

The Statutory Committee is given power in all cases with which it is concerned to impose a period of removal from the register, or disqualification, for a fixed time as well as indefinitely.

The Act makes it an offence for a person to take part in the publication of an advertisement calculated to lead to the use of the article advertised in the treatment of the following diseases: Bright's disease, cataract, diabetes, epilepsy or fits, glaucoma, locomotor ataxy, paralysis, tuberculosis (s. 8).

Advertisements published only so far as is necessary to bring them to the notice of certain named groups of people are exempt and also advertisements appearing in technical papers with a circulation mainly among a defined class of readers (s. 10).

The Act also makes it an offence to take part in the publication of an advertisement calculated to lead to the use of the article advertised for the purpose of procuring the miscarriage of women (s. 9). Advertisements in technical papers (as above) are exempted.

The Act requires that the composition of all medicines shall be disclosed with the exception of medicines made up according to a prescription for the needs of a particular person (s 11)

The method of disclosure is prescribed, the medicine as a whole may be named or, if this is not or cannot be done, each of the constituents or ingredients must be named. If the thing named is in the Poisons List, the name in the List must be used, if it is not in the Poisons List but is in the *British Pharmacopoeia* or the *British Pharmaceutical Codex*, the description at the head of the monograph must be used, in any other case the accepted scientific name or name descriptive of the true nature of the thing must be given.

Where the ingredients or constituents are named, the quantity present must also be stated.

The responsibility for the disclosure rests with the retailer but it is a defence to show that the seller did not know and had no reason to believe that the article was of a composition different from the declared formula (s 13).

Section 12 creates a group of 'authorized persons' who alone are entitled to sell medicines recommended for the treatment of human ailments. These persons include doctors, dentists, authorized sellers of poisons and persons who served a regular apprenticeship and were in business on their own account at the date of the passing of the Act. This last class represents a group of drug sellers who had certain privileges under the old Medicine Stamp Duties now repealed. The section prohibits the sale of any medicine accompanied by a recommendation from any place except a shop.

The section provides certain defences for other classes of sellers of medicines.

The effect of the whole of the provisions of the section is that drug sellers not coming within one of the named classes may sell (1) medicines with no recommendations attached, (2) proprietary medicines, with recommendations attached, excluding B.P. and B.P.C. preparations sold under a brand name, (3) herbs or mixtures of herbs, mixtures of herbs and water—with recommendations, (4) natural mineral waters or artificial imitations of them.

The Pharmaceutical Society has the duty of enforcing the whole of the Act (s 15) except section 12, which it has only the power to enforce. A food and drugs authority has the power to enforce sections 8, 9 and 11 (s 16).

The consent of the Attorney-General or the Solicitor-General is necessary to any proceedings for breaches of the Act except proceedings by the Society or by a food and drugs authority for a breach of section 11 (requiring the disclosure of the composition of medicines) (s 10 (4) and s 13 (3)). In Scotland the consent of the Attorney-General or the Solicitor-General is not necessary (s 18).

POLIOMYELITIS AND POLIOENCEPHALITIS

PATHOGENESIS

Portal of entry and path of transmission

Dangers of tonsillectomy

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During the season most favourable to the occurrence of poliomyelitis and despite the fact that the disease may not be prevalent, an operation such as tonsillectomy may allow poliomyelitis to develop. An instance of this is reported in a family of 6 children 5 of whom had tonsillectomy performed and extraction of teeth, in the month of August (Francis, Krill, Toomey and Mack). All these children became victims of bulbar poliomyelitis within 10 days and there were 3 deaths. It was not possible at the time to establish that there had been any contact with known local cases and there was not any epidemic, but subsequently the virus was recovered from 10 out of 54 specimens of faeces taken from distant contacts.

Nasopharynx

The view, once firmly held, that the virus passed from the nasopharyngeal mucosa by way of the filaments of the olfactory nerves to olfactory centres in the brain and onwards caudally to the spinal cord has largely been displaced so far as the disease in human beings is concerned.

Pharynx and intestine

The pharynx and intestine in man are now held to be the commonest portals of entry. Virus has been proved to exist in nasopharyngeal washings and in the faeces of active and convalescent patients as well as in those of abortive cases and contacts. Persistence of virus is unequal in different sites, the virus may remain up to the fifth day of the disease in the nasopharynx, but for as long as 4 months in the stools of convalescents. Carriers include convalescents, patients with abortive disease and contacts.

Central nervous system

Pathways to the central nervous system in man include neither the blood nor the cerebrospinal fluid, both are devoid of virus during the disease. Experimentally in the chimpanzee inoculated orally the transmission of the virus occurred along cranial nerves—fifth, seventh, ninth and twelfth—to their nuclei. Transmission from an

intestinal entry in man is as yet unproved, but in chimpanzees with inoculation confined to the intestine, lesions developed in the coeliac ganglia and the sympathetic chains of ganglia and in the spinal cord. Passage by the vagus through intestinal ganglia to preganglionic fibres of the vagus and thence to the brain is also a possibility (Howe and Bodian)

CLINICAL PICTURE

The pre-paralytic stage

Cerebrospinal fluid

A cell count in the first week of paralysis of from 50 to 200 cells, less often over 1,000, is common, falling rapidly to a normal figure by the end of the second week. Meanwhile the protein content, at first normal, mounts steadily to a maximum in about the third week 0.2 gramme in place of 0.03 gramme per cent.

The paralytic stage

The Kenny interpretation of infantile paralysis

So much has been said and written about the interpretation of infantile paralysis by Sister Elizabeth Kenny, not only in Great Britain but also in the United States of America, that it is advisable to summarize the main concepts. These are 3 in number: (1) There is muscular spasm of unknown origin present in the first few days of the disease, this is not the ordinary spastic condition associated with an upper motor neurone lesion; the difference is that the spasm does not relax when steady traction is applied to the limb. It is believed that the spasm causes anaemia and as a result there is fibrosis and contractures. (2) The term, mental alienation, is used by Miss Kenny and refers to functional or physiological blocking of impulses, as distinct from a lesion due to a purely anatomical obstacle. Sister Kenny explains the situation on a psychological basis. (3) Incoordination is to be explained in the first place as a sign that abnormal motor patterns have developed, these being interpreted as forms of substitution of impulses ('spilling over') to muscles which are not related to the affected muscle and which may even be in antagonistic groups. In the second place it is stated that a muscle may contract in a part of its structure instead of in the whole mass.

TREATMENT

The paralysis

The Kenny treatment

Before any claim can be allowed for the Kenny treatment the opinion of accredited observers must be carefully considered. Krusen has reported meticulously on his findings. In the first place he had talks with Sister Kenny and discovered that she had her own terminology; several American authorities (Steindler, Russin, Shepley and Wolkin) confirmed her findings, however. In the second place with regard to the treatment proper, the main elements are: (1) the application of hot packs so that spasm may be relaxed, once this has been accomplished; (2) the mental re-education of the patient so that he is induced to move the muscles voluntarily.

Stimson in discussing the Kenny treatment mentions that the action of the virus on the motor neurones does not necessarily result in their total destruction. If the affection is a temporary one the neurones concerned will recover their power but in the recovery stage the muscle fibres will be in a spastic condition. If there is complete destruction of the motor neurones paralysis is inevitable and incapable of cure, on the above hypothesis, however, the Kenny philosophy claims that if there are any surviving neuromuscular units they can be rescued. For these reasons there should be as little handling of the patients as possible in the early stages, splints should not be applied to limbs and there should not be any massage or electrotherapy. If a patient is in a dehydrated state and collapsed, intravenous transfusion of glucose-saline should be given. The application of hot fomentations when the muscles are in a state of spasm is said to be essential because spasm of the diaphragm, the pectoral muscles and the intercostal muscles is the main difficulty when there is respiratory interruption; it is stated that mechanical respirators actually aggravate breathing difficulties. Swallowing, micturition and defaecation are reflexes which are disturbed by spasm, these can be relieved by the application of hot fomentations. The rest of the treatment depends upon the careful introduction of passive movements and of active movements when spasm has passed off. The psychological element, however, is never lost sight of, the patient is always urged to make the adjustments necessary to the situation.

Francis, T., Jun., Krill, C. E., Toomey, J. A., and Mack, W. N.
(1942) *J. Amer. med. Ass.*, **119**, 1392.

Howe, H. A., and Bodian, D. (1942) *Neural Mechanisms in Poliomyelitis*. New York and London.

Kenny, Elizabeth (1941) *The Treatment of Infantile Paralysis in the Acute Stage*. Minneapolis.

Krusen, F. H. (1942) *Proc. Mayo Clin.*, **17**, 449.

Steindler, A., Russin, L. A., Sheplan, L., and Wolkin, V. (1942) *Arch phys Ther*, 23, 325
Stimson, P. M. (1942) *J Amer med Ass*, 119, 989

PREGNANCY NORMAL AND PATHOLOGICAL DIAGNOSIS OF PREGNANCY

The Hogben test

- 1292 The clawed toad (*Xenopus laevis*) is used. Its advantages over the Aschheim-Zondek and Friedman tests are that (1) a result can be obtained in from 6 to 15 hours, (2) the toads are not killed, and can be used over and over again, (3) ovulation does not occur apart from a mating with a male, and so the animals do not need to be isolated. If the test is positive, a shower of ova is ejected and are easily recognized by the naked eye.

HAEMORRHAGES

Unavoidable haemorrhage from placenta praevia

Treatment

- 1295 Browne now considers that the use of the Willett forceps (as described in Vol X, p 81) is inadvisable in placenta praevia, as infection with *Clostridium welchii* has followed its use in 2 cases, in one of which the mother died. In using the forceps a wound is made on the foetal scalp, and the compression of the placenta by the continuous weight-traction is apt to kill the foetus, conditions then are ideal for infection by *Cl. welchii*, namely, a lacerated wound in dead tissue. Absence of *Cl. welchii* from the vagina and skin of the perineal region can never be assured, as the organism is very widely disseminated in maternity hospitals.

HYPEREMESIS GRAVIDARUM

Treatment

- 1296 Stress is laid on the administration of vitamin B₁, which should be given daily in the form of aneurine hydrochloride, 2 milligrams subcutaneously, intramuscularly, or intravenously. A careful look-out should be kept for dimness of vision, and the fundus oculi should be examined at short intervals for evidence of optic neuritis or retinal haemorrhages. The appearance of either of these calls for the immediate termination of pregnancy.

TOXAEMIAS OF LATE PREGNANCY

Pre-eclamptic toxæmia and eclampsia

Clinical picture

- 1297 Abnormal increase in weight during pregnancy has been regarded as such a reliable sign of toxæmia of pregnancy that the latter could be diagnosed from it alone. From an investigation of 100 cases with definite toxæmia of late pregnancy, Siddall and Mack conclude that an excessive increase of weight is of doubtful value as a warning of the toxæmia of pregnancy and only of secondary importance in its diagnosis. Their patients showed an average gain of 17 pounds during the last 4 lunar months of pregnancy compared with the normal 15.7 pounds. Of their 100 patients 61 showed gains of weight at least twice the average of controls at one or more observation periods during this time, but a similar gain in weight also occurred in 45 per cent of the normal pregnancies. Sudden increase of weight was somewhat more frequent among toxæmic than among normal pregnancies, but was far from constant. The presence or absence of excessive gains in weight did not bear any relation to the type or severity of the toxæmia.

Course and prognosis

Remote prognosis—The remote prognosis of the various conditions classified under pregnancy toxæmias has been studied by Browne and Dodds by following up a series of 400 patients in 589 pregnancies during periods varying from 12 years to 6 months. The results were briefly as follows. Of 144 patients who had pre-eclamptic toxæmia 50 per cent developed permanent hypertension and 50 per cent recovered completely. In no case did chronic glomerular nephritis supervene. After eclampsia residual hypertension was observed in 60.8 per cent. The older the patient in both these conditions, the greater her parity, the higher the blood pressure during pregnancy and the longer the duration of the illness before delivery, the greater was the liability to the ultimate occurrence of residual hypertension. Browne and Dodds did not find any evidence to support the view that chronic glomerular nephritis is a late result of either pre-eclamptic toxæmia or eclampsia. Of patients who had hypertension before pregnancy began 9.2 per cent were dead at the end of the 12-year period. Nevertheless the majority of patients who have pregnancy superimposed on simple hypertension pass through the pregnancy without any demonstrable permanent deterioration of their general condition.

Chronic glomerular nephritis is a rare complication of pregnancy and in the 12-year period there were only 17 patients in 19 pregnancies. The ultimate prognosis is usually bad and 29.4 per cent of the patients were dead by the end of the 12 years. Pregnancy was always a serious risk in these patients and should not usually be

allowed to continue. In about 50 per cent of the cases, however, the patient did not seem to be any worse as a result of it. These were mostly mild cases with satisfactory kidney function.

Recurrent toxæmia is usually due to a persistent hypertension, often of slight degree, between pregnancies. This was usually a sequel to a previous pre-eclamptic toxæmia or eclampsia and when a new pregnancy took place the hypertension was always liable to undergo exacerbation, the blood pressure rising to 160 or over. Albuminuria and oedema often followed this rise of blood pressure and if not adequately and promptly treated foetal death was apt to occur in utero or perhaps premature labour.

Siddall, R. S., and Mack, H. C. (1938) *Amer J Obstet Gynec*, **36**, 380

PROSTATE DISEASES

SIMPLE ENLARGEMENT

Treatment

Transurethral prostatic resection

Although in Great Britain the transurethral method of prostatic resection is not popular, the very opposite has to be reported with regard to the United States of America where, for instance, in 1940 and 1941 there were 4,302 cases dealt with by this method. Actually in 1941 not one patient was treated by perineal or suprapubic prostatectomy at the Mayo Clinic. The average age of the patients was 66.2 years, and 4.3 per cent were 80 years of age or more. There were only 2 deaths in the latter group (85 patients). For the rest, in nearly one thousand operations the death rate was just over 1 per cent.

1308

MALIGNANT DISEASE

Treatment

The best hope of success in treating the malignant prostate lies first in the making of a diagnosis sufficiently early to allow of its being enucleated and secondly in the adoption of hormone therapy. Unfortunately a diagnosis can rarely be made so early that the total extirpation of the disease is feasible, and this being so, treatment will usually consist of relieving obstruction and of either carrying out subcapsular orchidectomy, or of administering oestrogens. Even although no permanent cure has yet been reported from these new remedies, they offer the best hope of ameliorating the condition of the patient with carcinoma of the prostate.

The treatment of carcinoma of the prostate may be considered under three headings, surgical, radiotherapeutic and hormonal.

Surgery

British surgeons are of the general opinion that by the time the malignancy of the prostate is clearly established, it is too advanced to allow of its being successfully removed. So long as the disease remains confined within the capsule the prostate is generally believed to be an innocent one, its true nature only being discovered by microscopical examination after it has been enucleated. The surgical treatment of the diagnosed malignant prostate in Great Britain is therefore generally confined to the adoption of measures for the relief of obstruction. Here the surgeon has two choices, namely the establishment of a permanent suprapubic drainage and the carrying out of a perurethral resection. In spite of the possibility that the use of diathermy may stimulate growth, resection has become the treatment of choice whenever measures have to be undertaken for the relief of retention. The results have been on the whole satisfactory, especially when resection is combined with the other forms of treatment described below.

Radiotherapy

Two varieties of cancer radiotherapy have been employed, the implantation of radium needles and deep X-ray therapy. At a meeting of the Radiotherapy Section of the Faculty of Radiologists held in 1943 the results in 87 cases in which radiotherapy was used were reported by Williams. In no case was the progress of the disease completely arrested but the average duration of life was increased and the results of X-ray therapy were said to be preferable to those obtained by the use of radium. In spite of this statement, it has to be admitted that radiotherapy has proved to be less successful in the case of carcinoma of the prostate than it has been in the case of the somewhat analogous condition of carcinoma of the breast.

Hormone therapy

Hormone therapy is undoubtedly the form of treatment which is of greatest interest at the present moment. It is based on the observation that the prostate is sensitive to androgens and oestrogens. For example, the growth of the prostate can be stimulated in many animals prior to puberty by means of androgens, and after puberty enlargement can be induced by the giving of oestrogens. An examination of the prostatic fluid of a dog also shows that it contains two enzymes, fibrolysin and phosphatase. The amount of acid phosphatase in the prostate increases at puberty and remains high until senescence. This enzyme is present in the blood stream and

the amount found in human serum is increased in cases of carcinoma of the prostate Huggins, to whom we owe this pioneer work in hormone therapy, also discovered that the amount of acid phosphatase fell when the patients concerned were given injections of oestradiol benzoate (Huggins, Stevens and Hodges) This fall was associated with a considerable improvement in the clinical condition of the patient Later Huggins, Scott and Hodges tested the action of stilboestrol and hexoestrol, which have the advantage that they can be given by the mouth, and they obtained similar results A great many subsequent workers have made use of these discoveries and oestrogen therapy is now being extensively used in the treatment of the malignant prostate Nobody who has employed this method of treatment has claimed that it is capable of producing a permanent cure, but that temporary relief often results from it can no longer be disputed Not only does the primary focus in the prostate often regress, but the distressing symptoms resulting from the existence of metastases are distinctly alleviated A patient who is bedridden not infrequently becomes active again, puts on weight, loses his pain and believes that he is on the road to recovery How long this improvement is likely to be maintained cannot yet be assessed, but many a patient has been given an extra 6 or 12 months of reasonably comfortable life by this new form of therapy No untoward effects have yet been noted from the giving of oestrogen beyond the occasional development of a mild mastitis The dosage should be controlled not only by this sign, but also by the routine estimation of the acid phosphatase in the blood Huggins regards 3.2 units per 100 cubic centimetres as the normal upper limit of acid serum phosphatase, from 5 to 10 units as suspicious of prostatic cancer, and over 10 units as indicative of the existence of metastases The usual dosage of stilboestrol is in the neighbourhood of 1 milligram 3 times a day and as much as a total of 3,000 milligrams has been given in 11 months

Castration

The alternative method to hormone therapy, namely that of castration, has advantages over oestrogen therapy but there are also disadvantages The main advantage is that it obviates the necessity of continually taking medicine and the chief disadvantage that it necessitates an operation, and an operation to which many patients strongly object The psychological repercussions of the loss of the testicles may, however, be prevented by adopting the subcapsular method of orchidectomy In this, the tunica albuginea is opened and the testicular tissue eviscerated, leaving behind the epididymis and the capsule of the testis If the patient is told beforehand that only parts of the testicles are to be removed, his objection to the operation will be diminished

- Huggins, C, Scott, W W, and Hodges, C V (1941) *J Urol*, **46**, 997
— Stevens, R E, Jun, and Hodges, C V (1941) *Arch Surg*,
Chicago, **43**, 209
Williams, I G (1943) *Brit J Radiol*, **16**, 190

PSITTACOSIS

AETIOLOGY

Causal agent

The virus of psittacosis

- 1311 Bedson discusses the morphology of the virus of psittacosis, and the aetiology of the disease Previously it has been thought that only the psittacine species in nature constituted the primary host and suffered from the disease, but recent work has shown that the atypical cases of pneumonia which have occurred in the Faroe Islands, where the islanders eat salted fulmar petrel fledglings, were probably caused by a virus identical with that causing psittacosis The serums from 5 out of 7 patients fixed complement in the presence of a psittacosis antigen, the 2 negative serums were from clinically doubtful cases

Haagen and Mauer isolated from the young petrels and from the human cases a virus which was indistinguishable from psittacosis virus More recently, serum from 5 cases of a similar disease which occurred in Iceland, where petrels are used as food, gave a positive psittacosis complement fixation test It is suggested that the relative failure of the control on the importation of parrots and parakeets is due to the fact that apparently healthy birds may be carriers, that home stocks are infected and that parakeets and budgerigars are susceptible, the latter often acting as carriers after suffering subclinical attacks, for detection of such infection the complement fixation test of Meyer and Eddie will be available

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Serological diagnosis

Complement fixation test

For this boiled antigen is the most satisfactory The antigen is best prepared from tissue culture virus purified by fractional centrifugation and tryptic digestion

- Bedson, S P (1940) *Lancet*, **2**, 577

PSITTACOSIS—PSYCHONEUROSES AND PSYCHOTHERAPY

Haagen, E, and Mauer, G (1939) *Dtsch med Wschr*, **65**, 13
Meyer, K F, and Eddie, B (1939) *J infect Dis*, **65**, 225

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KEY NUMBERS
1311

PSORIASIS

AETIOLOGY

It should be stressed that psoriasis is less common not only in the coloured races but also in the white population living in warm dry climates. The fact should be appreciated, however, that a white person suffering from psoriasis will not necessarily be cured by going to live in such a climate.

1312

TREATMENT

A very comprehensive review of the present position as regards aetiology and treatment of psoriasis is given by Wise and Sulzberger. Further studies of lipoid metabolism have not, in the main, supported the contention of Grutz and Bürger that psoriasis is an evidence of lipoidosis and treatment directed along these lines has not been fruitful. Sulphonamide therapy occasionally has a beneficial effect, generally in those cases which are acute and generalized and follow septic infections of the throat (MacCormac).

Vitamin therapy has been similarly disappointing in spite of some evidence suggesting a deficiency of vitamin C (Reiss). Heavy dosage of vitamin B₁ and of vitamin D have been reported as exercising a beneficial effect on psoriasis, but except where these measures are indicated by other symptoms they do not appear to be of any absolute value in psoriasis. This aspect of the problem has been reviewed by Madden. **Goeckerman's treatment**

Goeckerman's treatment of psoriasis consists essentially in the application of tar paste at night which is lightly removed with oil in the morning, thereafter the patient is exposed to ultra-violet rays. The treatment is most successful when the patient is in hospital.

Dithranol

Cignolin (dithranol) is also very effective in the treatment of psoriasis and an ointment made up by mixing 2 grains of cignolin in Lassar's paste is to be recommended. The paste should be removed every morning while the patient is in a tar bath, the bath consisting of 4 ounces of liquor picis carbonatus to thirty gallons of water. After the bath the patient is exposed to ultra-violet light until erythema is produced and then the paste is applied once more. If the patient is in hospital the treatment will commonly clear psoriasis in from 10 to 14 days.

MacCormac, H (1940) *Brit J Derm*, **52**, 339

Madden, J F (1940) *J Amer med Ass*, **115**, 588

Reiss, F (1938) *Chin med J*, **53**, 141

Wise, F, and Sulzberger, M B (1939) *Year Book of Dermatology and Syphilology*, p 1 Chicago

PSYCHONEUROSES AND PSYCHOTHERAPY

PSYCHONEUROSES

Psychopathology

Reactions to difficult situations

Importance of predisposition—All writers seem to be agreed on the importance of predisposition in psychoneurosis arising out of the present war, whether in members of the Forces or in civilians. The proportion found varies in accordance with differences in the standards adopted by the observers, and in their opportunities and more especially in accordance with the kind of material observed. Thus, in a psychiatric hospital in Great Britain with troops under training conditions predisposition has been described in 82 per cent (Hadfield), whereas among Australian troops at Tobruk 35.2 per cent were regarded as having had some kind of predisposition (Love). In 63 Civil Defence workers with 'subacute' psychological symptoms after an air-raid 48 per cent were found to be considerably predisposed (Wilson). The predisposition described is usually in the family history, or in a history of 'nervous breakdown', of previous neurotic symptoms, of chronic physical complaints for which a definite organic cause has not been found, or of frequent changes of job, but there are many other factors to be taken into account, such as over-dependence on home, including some that require time and special experience to elicit. These observations reinforce the view that psychiatric selection, if it can be done adequately, should be of great value, both as a preventive of psychoneurotic and other forms of psychological breakdown, and as a means of increasing the efficiency of any Service, either by rejecting the unstable or by placing them in jobs familiar to them from civilian experience or suited to their aptitudes. The armed Forces now submit all their recruits to a group intelligence test, rejecting individuals with the lowest score only after a psychiatric examination to confirm the value of the group score, and to ascertain the man's or woman's actual employment history and other facts bearing upon stability of temperament and predisposition generally. This method does not pick out the majority of the potential psychiatric casualties, but it eliminates a pro-

1315

portion of them, and it allows the dull man to be allotted to duties within his capacity, for example in the Army to the armed or unarmed pioneers, according to his degree of dullness of intelligence. The same principle in a different form can be applied to the upper end of the scale, in the selection of officers, but the relevance to fighting capacity has still to be demonstrated in the experiences of the battlefield (Rees)

PSYCHOTHERAPY

General treatment

Importance of rest

- 1316 As regards treatment the war has brought home an old truth—the value of rest in the treatment of many psychiatric casualties. Mild depressions, especially in people of obsessional temperament, anxiety states whether in fighting men or Civil Defence workers or industrial employees who have long worked overtime, will often clear up with a few weeks' good well-arranged rest, and little else. It is worth remembering that war is more productive of fatigue in most people than is peace because of the spurts of special effort which are more characteristic of the fighting man and which, because of the long continuous overwork, are apt to be the lot of some civilians. Nine-tenths of the psychiatric battle casualties in the Middle East, according to Craigie, turned out to be states of exhaustion, and the patients concerned, after about 48 hours' rest, aided by sedatives if need be, were restored to the normal. It is quite likely, however, that doctors have often overlooked the share of the same factor in producing psychoneurotic forms of illness in peace-time, not only in the poorer but also in the middle classes, especially with regard to the mothers.

Sedatives

In the more severe psychological upsets more drastic methods are applicable. Panic indicates the use of a sedative sufficient to produce sleep for the greater part of 24 hours. Paraldehyde, 4 drachms, sodium amytal, 3–6 grains, nembutal, 3–4 grains by the mouth—all of them capable of repetition to some degree after 4 or 6 hours—are recommended, not only with the object of relieving symptoms of acute panic, but in the hope of preventing the development of a chronic state of anxiety (Sargant). It is possible that emergency treatment of this sort may have some prophylactic value by limiting the impressions made by the disturbing event—partly by preventing ruminations and partly by a more direct physiological effect. The intravenous route may be used in the barbiturates, and the result is produced more quickly. When chronic anxiety symptoms of a severe degree persist, continuous narcosis has been recommended, but this can be carried out only in a hospital with a specially trained staff as the treatment is not without risk. For individuals of good material who have broken down under severe stress, with loss of weight, an insulin fattening technique has been used (Sargant), but while it helps the patients physically and also gives them encouragement it does not seem to make them able to return to active service in any greater proportion than does a well-planned rest period.

Hadfield, J. A. (1942) *Brit med J*, 1, 281, 320

Love, H. R. (1942) *Med J Aust*, 2, 137

Rees, J. R. (1943) *Brit med J*, 1, 1

Sargant, W. (1942) *Brit med J*, 2, 574

Wilson, H. (1942) *Lancet*, 1, 284

PSYCHOSES. I.—AFFECTIVE PSYCHOSES

CLINICAL PICTURE

Depression

Depressive states in war

- 1319 Depressive states proved to be extremely common in psychiatric casualties both in the Navy and in the Army. The diagnosis is one more commonly made than that of hysteria, in striking contrast to experience in the war of 1914–18. It is probable that the difference is not so much in the relative frequency of these two clinical pictures, as in the judgment and attitude of the psychiatrist. In a naval neuropsychiatric unit 13 per cent of the cases admitted were diagnosed as states of depression (Curran and Mallinson), and 25 per cent of 274 consecutive cases admitted to a military hospital for psychotic soldiers were diagnosed as states of depression (Tredgold). Interest in the psychogenesis of depressive states (see Vol. X, p. 272) has accordingly been greatly stimulated. Curran and Mallinson tried to classify their 88 naval patients with depression into endogenous and reactive types, according to the part played by constitutional predisposition and external stress. Tredgold made a similar attempt, using differences in the clinical picture as criteria. None of these investigators found it possible to draw any clear line between endogenous and reactive types of depression, and would rather regard the material as making a graded sequence, each case differing from the preceding only in the

degree to which constitutional or environmental factors were important. The age of the naval patients was over 35 years in 63 per cent, and in other ways the clinical picture resembled that seen in civil life. There were, however, some significant differences. Physical factors were often prominent as a contributory cause of the illness (23 out of 88 naval patients), dullness or mental defect was also found with excessive frequency by peace-time standards, being seen in 18 of the naval and in 21 of the military patients, the average duration of the illness (4-6 months) was also shorter than the course usually observed in peace-time. Curran and Mallinson considered that although their patients responded favourably to psychological management, reassurance, and psychotherapy, there was a danger of the hysterical prolongation of invalidism by the desire to escape further stress. The outlook in these cases was fairly good, but not always entirely favourable. Only 29 per cent of the naval patients returned to duty, and although nearly all recovered, 26 per cent showed some reduction of their previous working capacity after discharge, and 6 per cent needed further hospital care. The proportion of military patients returned to duty is, unfortunately, not stated, but 59 out of 70 made a complete clinical recovery. Apart from a few cases treated with continuous narcosis, no special method of physical treatment was employed in either of these groups. An increase of depressive illnesses in the civil population exposed to bombing has not been reported. Brown observed a few cases of depression, but no case of mania, occurring in middle-aged or elderly people as a result of air attacks.

TREATMENT

Symptomatic*Prefrontal leucotomy*

In 1936, Moniz introduced prefrontal leucotomy as a therapeutic measure for numerous mental disorders, excluding dementia. Recently the treatment has been used more especially for cases of depression or for anxiety states. The operation produces euphoria without obvious personality changes but there is some impairment of abstract thinking and the patient's increased cheerfulness may give rise to errors of tact, lack of self-consciousness and reduction of initiative and spontaneity have been noted as after-effects.

Specific*Convulsion therapy*

The favourable effects of convulsion therapy in depressive psychoses, and especially in involuntional melancholia, have been confirmed, although the published work on the subject is still very small. Cheney, Hamilton and Heaver have treated 51 manic-depressives and 16 patients with involuntional melancholia with convulsions induced by injection of leptazol (cardiazol). Of the 51 manic-depressives, 29 recovered sufficiently to return home, 19 improved but remained in hospital, and only 3 did not improve. Of the 16 involuntional 13 went home, 2 remained in hospital improved, and one patient showed no improvement. The introduction of convulsions produced by electrical means (Bini and Cerletti) has very much simplified the technique and robbed it of most of its disagreeable features. Electrically produced fits have much less effect on the heart than has the use of analeptic drugs such as leptazol and triazol, the tachycardia following the convulsion is of shorter duration and no case in which cardiac damage has occurred has been reported. The application of this method of treatment to middle-aged patients and even to out-patients (Strauss and MacPhail) seems to be justified. The electrical discharge produces an immediate loss of consciousness, with subsequent complete loss of memory for the whole of the operation, whereas when the fit is produced by the injection of a drug there are very unpleasant premonitory symptoms which are remembered subsequently by the patients and often cause great reluctance to undergo the experience again. It seems probable, moreover, that the risk of accidents is less with the use of the electrical method.

Mania appears to respond much less readily than does depression to convulsion treatment, but the method might be employed in chronic patients, particularly those showing some confusion. A manic or hypomanic state occasionally supervenes after the convulsion treatment of a case of depression. The elation lasts for only a few days as a rule but Mayer-Gross observed mania of a severity sufficient to necessitate admission to hospital, this complication occurred in a young woman who was being treated for only a mild depression in an out-patient department.

Bini, U., and Cerletti (1938) *Boll. Accad. med., Roma*

Cheney, C. O., Hamilton, D. M., and Heaver, W. L. (1941) *J. nerv. ment. Dis.*, **94**, 344

Curran, D., and Mallinson, W. P. (1941) *Brit. med. J.*, **1**, 305

Moniz, E. (1936-7) *Amer. J. Psychiat.*, **93**, 1379

Strauss, E. B., and MacPhail, A. (1940) *Brit. med. J.*, **2**, 779

Tredgold, R. F. (1941) *Brit. med. J.*, **2**, 109

PSYCHOSES III—SCHIZOPHRENIA
TREATMENT

Specific

Cardiazol convulsion therapy

- 1321 In an attempt to elucidate the mechanism of the convulsion after the administration of leptazol (cardiazol), Denysen and Watterson experimented with appropriate doses of various vaso-depressant drugs—amyl nitrite, sodium nitrite, and histamine, given immediately prior to the known convulsion-producing dose of cardiazol. The subjects were 32 schizophrenics in good physical health. These measures mainly prevented convulsions, demonstrating the fact that vasodilatation, under appropriate conditions, prevents their occurrence. The action of leptazol on the cardiovascular and central nervous systems is reviewed, and it is concluded that leptazol-produced convulsions are due to sudden vasoconstriction.

Results obtained by American and European authors from treatment of schizophrenics with leptazol have been analysed by Reitmann. The analysis was difficult owing to differences in classification adopted by the various authors and in their estimations of what constituted a remission of the disease. Reitmann found that there were 52 per cent of full remissions, with a standard deviation from the mean of 3.8 per cent. This figure agrees with that of other observers, it includes only acute and subacute cases, as in chronic cases nothing more than arrest of the disease can be expected and in cases of more than 6 or 7 years' duration the prognosis is hopeless.

Electrical convulsion therapy

This form of convulsion therapy is now widely in use because it causes the minimum of discomfort to the patient and there are few if any complications—always provided that the administration of the treatment is in efficient hands. Lewis says 'electrically induced convulsion therapy appears to be a safe and convenient method of treatment'.

Denysen, J. A. F., and Watterson, D. J. (1938) *J. ment. Sci.*, **84**, 1002.

Lewis, N. D. C. (1943) *Bull. N. Y. Acad. Med.*, **19**, 227.

Reitmann, F. (1939) *Lancet*, **1**, 439.

PSYCHOSES. IV.—TOXIC INFECTIVE PSYCHOSES

CLINICAL PICTURE

- 1322 The clinical pictures described in the original work (Vol. X, p. 319) are often called 'symptomatic psychoses' because they are symptomatic of some physical disorder in the body. The difficulty of basing on them the diagnosis of the underlying disturbance was explained by their lack of specificity. Considering their name, toxic infective psychoses, it is worth recalling that their occurrence is not limited to toxic and infective conditions unless one stretches these terms until they lose any specific meaning. Among the infective conditions there is a certain tendency for some to give rise to symptomatic psychoses, whereas others rarely produce mental symptoms (Vol. X, p. 318), and this difference may be used diagnostically. The important point, however, is that the psychosis may be the first symptom, preceding any physical manifestations. By remembering that the picture as described is diagnostic of 'physical disease', and therefore being on the look-out, the diagnosis should not be missed.

The mental changes produced by low oxygen pressure belong clinically to the group of symptomatic psychoses, they have become of great practical importance in high altitude flying, and can be produced experimentally in the low-pressure chamber. If the anoxia comes on gradually, difficulty in concentration, incoherent thinking, and slowing down of all mental processes may introduce the picture. Very early it is characterized by lack of subjective awareness of the disturbance up to complete loss of insight. This feature makes the later stages reminiscent of a severe alcoholic intoxication, and this the more so as the patients are often euphoric and quarrelsome, singing or shouting, and obstinately refuse to take orders which may be essential for their safety. Grasp and judgment are severely disturbed in these states, and subsequent amnesia, or patchy recollection of the events during the period of anoxaemia, prove the clouding of consciousness in retrospect.

PUERPERIUM

PHYSIOLOGY OF THE PUERPERIUM

Superinvolution

- 1326 If treatment by ovarian hormones is indicated, the synthetic oestrogen stilboestrol may be administered orally.

MANAGEMENT OF THE NORMAL PUERPERIUM

After-pains

Treatment

- 1327 *Testosterone*—Painful uterine contractions may be successfully treated by the use of testosterone and allied substances (Abarbanel¹).

Posture

Postnatal exercises are of use in promoting involution and convalescence (Wilson)

1327

Painful engorgement of the breasts*Treatment*

Testosterone —Mammary engorgement is controlled by testosterone, 25 milligrams being given by injection every 12 hours until a total of 125 milligrams is reached. Methyl testosterone may be given by the mouth, preferably sublingually, but the dose required is about four times the amount of testosterone propionate when given intramuscularly (Spence). This treatment has not any effect upon lactation, in contrast to stilboestrol therapy which has a similar effect upon engorgement but inhibits glandular activity (Abarbanel², Stewart and Pratt, Lass).

COMPLICATIONS OTHER THAN SEPSIS**Bladder complications***Retention of urine*

In the treatment of retention, injection of mecholyt or doryl may be of value as a preliminary, or alternative, to catheterization

1328

Cerebral thrombosis after childbirth

Thrombosis in the superior longitudinal sinus occurs in the puerperium and gives rise to signs of intracranial pressure or of obstruction of the superior cerebral veins. The thrombosis may be primary in the sinus itself, but most commonly it is secondary to venous thrombosis elsewhere, particularly in the femoral and pelvic veins. Batson has shown that the pelvic veins anastomose freely with the veins in the vertebral canal and thus communicate with the dural sinuses. He deduced, from his experiments on animals, that during coughing and straining, blood was squeezed out of the abdominal veins into the vertebral system and so upwards towards the cerebral sinuses. This work has an obvious bearing upon the treatment of pelvic and femoral thrombosis in puerperal women. The normal circulation through the vena cava must be promoted by exercises, every precaution must be taken to avoid straining, the abdominal binder must be discarded, and the patient must be nursed in the Fowler position (Symonds, Martin, Martin and Sheehan).

Treatment

Stansfield recommends the following treatment when thrombosis has taken place: (1) Heparin given by continuous intravenous drip in normal saline of 50 per cent glucose solution. (2) The reduction of intracranial pressure by lumbar puncture and intravenous injections of 50 per cent glucose or intramuscular injections of 10 cubic centimetres of 20 per cent magnesium sulphate. (3) Control of the fits by chloroform anaesthesia at the outset and subsequently by avertin given by the rectum.

Shock*Pituitrin shock*

It has been shown that pituitrin shock is not necessarily due to contamination of the pituitary preparation by histamine, and that it may be due to anaphylaxis or to cardiac failure resulting from constriction of the coronary artery. Discretion must be exercised in the employment of this drug, and other oxytocic agents should be used whenever possible. If repeated injections of pituitrin are necessary, small doses only must be given (for example 10–15 units). The constricting action upon the coronary arteries may be avoided by combining pituitrin with ephedrine, and great care must always be taken to avoid a vein when the injection is being made. Pituitrin is absolutely contra-indicated in the presence of coronary disease. The treatment of the manifest condition consists of the administration of adrenaline (ephedrine) together with intravenous fluids and oxygen, except for patients under ether or cyclopropane anaesthesia, when adrenaline and ephedrine are contra-indicated, and treatment must be limited to the giving of fluids and oxygen (Adelman and Lennon).

Necrosis of the pituitary gland

Sheehan and others have drawn attention to the occurrence of post-partum necrosis of the anterior lobe of the pituitary gland in women who have suffered from serious collapse during or after delivery. The necrosis is ischaemic in origin and is most commonly due to post-partum haemorrhage, but other causes of serious collapse, such as heart disease or toxæmia, may be predisposing factors. The lesion is not in itself directly fatal, and although many of the patients die, they die from shock, sepsis or some other complication, and not from pituitary failure. In the patients who survive, the after-effects depend upon the amount of necrosis and the degree of hypopituitarism resulting therefrom. In minor degrees of damage there may not be any sequelae. When the amount of damage is such as to cause a severe degree of pituitary deficiency, a clinical syndrome is set up which includes hypomenorrhoea, sterility and adiposity. Superinvolution of this type may respond to hormone therapy, and the necessity for such treatment should be borne in mind.

1328

whenever severe haemorrhage or collapse is followed by signs of hypopituitarism. In cases in which a very large amount of the gland is destroyed, the asthenia, anorexia and emaciation which are characteristic of Simmonds's syndrome may supervene

PUERPERAL SEPSIS

Bacteriology

1329

Transference of infection to genital tract

Cruickshank and Godber investigated the method of spread of streptococcal infections, including two small outbreaks of puerperal sepsis, and collected evidence of the importance of aerial spread and of dust-borne infections. In some cases of puerperal sepsis examination of all contacts for carriers is negative, and in such cases the authors believe that an infected atmosphere or infected dust is the source of the infection. In one of their investigations exposure of a blood-agar plate in a ward, from which an infected patient had been removed 6 days previously, provided haemolytic streptococci of the same type as that recovered from the patients in this epidemic. To prevent the spread of organisms by this means, free ventilation of wards, damp sweeping and dusting, and a liberal use of soap and water are effective, sterilization of the air and dust by spraying with aerosols or by ultra-violet irradiation is more expensive, and probably no more effective.

Treatment*Prevention*

The dazzling achievements of modern chemotherapy have tended to create a false sense of security and to distract attention from the less spectacular methods of prevention which, nevertheless, remain the most important. To summarize the main preventive methods, the three most outstanding are first, efficient care in the antenatal period with special attention directed to physical fitness, and to the state of the blood particularly, secondly, satisfactory conduct of the confinement itself, having regard to all the essentials, and thirdly, shielding of the patient against infective organisms during the puerperium (Greenhill). Baird quotes the statement made by Dora Colebrook, namely that in half of the number of cases of haemolytic streptococcus infection the person in attendance on the patient—doctor, nurse, midwife—is responsible for the puerperal sepsis himself or herself.

As the vagina is the most fertile cavity for the development of the streptococcus it is becoming more and more the rule that examination should be made per rectum instead of per vaginam.

Specific chemotherapy

The dangerous toxic effects which may follow the administration of sulphanilamide must be emphasized, as reports of the occurrence of agranulocytosis are increasing in frequency. The experience gained in the prevention and treatment of this complication at Queen Charlotte's Hospital, London, was summarized by Colebrook, who points out the risk of overlooking the condition because of its insidious onset, and also the high mortality, more than 50 per cent in the recorded cases. Most of the cases of agranulocytosis have followed treatment with sulphanilamide, 6 have been recorded after sulphapyridine, and one after prontosil rubrum. In all except 2 cases 30 grammes at least of the drug had been given, as the dose necessary to control a severe streptococcal infection is between 20 and 30 grammes, the margin of safety is very small. Colebrook considers that, if a patient does not improve during the first 5 or 6 days of treatment, the causal organism is probably not sensitive to the drug. During these first 6 days, if the patient is improving and the fever subsiding, leucocyte counts are not necessary but if the temperature does not fall or if there are any disturbing symptoms, such as headache, leucocyte counts should be made every second or third day. Whenever more than 25 grammes are administered, or the treatment is prolonged for more than 10 days, leucocyte counts should be made at short intervals.

Abarbanel, A. R. (1939)¹ *Amer J Obstet Gynec*, **38**, 243

— (1941)² *ibid*, **42**, 110

Adelman, M. H., and Lennon, B. J. (1941)³ *Amer J Obstet Gynec*, **41**, 652

Baird, D. (1942) *Practitioner*, **148**, 134

Batson, O. V. (1940) *Ann Surg*, **112**, 138

Colebrook, L. (1939) *Lancet*, **2**, 158

Cruickshank, R., and Godber, G. E. (1939) *Lancet*, **1**, 741

Greenhill, J. P. (1942) *Year Book of Obstetrics and Gynecology*
Chicago

Lass, P. M. (1942) *Amer J Obstet Gynec*, **43**, 86

Martin, J. P. (1941) *Brit med J*, **2**, 537

— and Sheehan, H. L. (1941) *Brit med J*, **1**, 349

Sheehan, H. L. (1940) *Lancet*, **2**, 321

Spence, A. W. (1942) *Brit med J*, **1**, 668

PYELITIS—RADIOLOGY IN DIAGNOSIS AND TREATMENT

- Stansfield, F R (1942) *Brit med J*, 1, 436
Stewart, H L, Jun, and Pratt, J P (1941) *Amer J Obstet Gynec*, 41, 555
Symonds, C P (1940) *Brit med J*, 2, 348
Wilson, J St G (1937) *Pre-natal and Post-natal Management*
London

PYELITIS

TREATMENT

Cure

Subacute and chronic pyelitis

The use of sulphonamide drugs has greatly extended (see below)

1330

PYELITIS OF PREGNANCY

Treatment

Sulphanilamide continues to hold an important place in the treatment of pyelitis of pregnancy. It is more quickly effective than any other standard treatment in pyelitis of pregnancy, a dosage of 0.5 gramme 3 times daily rapidly produces a remission of symptoms and in simple cases the urine becomes sterile in from 4 to 5 days. In toxic and severe cases of pyelitis larger doses and more prolonged treatment are necessary in order to sterilize the urine. Further, the treatment of patients with pyelitis of pregnancy by sulphanilamide is associated with fewer complications than is any other treatment, for example premature onset of labour is rare and the children born are often of normal weight. This is in contradistinction to the frequency of onset of premature labour (about 30 per cent) and the high still-birth rate and neonatal mortality from underweight and feebleness of the infants when sulphanilamide has not been used.

1331

PYLORIC OBSTRUCTION

HYPERTROPHIC STENOSIS OF THE PYLORUS

Treatment

Choice of medical and surgical treatment

Paterson discusses the treatment of congenital pyloric stenosis and concludes that surgery remains the method of choice for all but selected cases, especially in very young infants who show progressive loss of weight after 8 weeks of age. Barrington-Ward discusses the management of cases of pyloric stenosis and considers that the claims of surgery as a treatment are strong, in 1939 the mortality rate at the Hospital for Sick Children, Great Ormond Street, London, was only 6.5 per cent.

1334

Eumydrin—When weight is being maintained a trial of eumydrin should be made, and the drug is more likely to give good results in females than in males, it is best given in the form of lamellae or in concentrated alcoholic solution (Paterson). Dobbs reports that eumydrin can be used successfully as a method of out-patient treatment. Eumydrin medication may be suitable in mild cases of pyloric stenosis, or for conditions which do not begin until the third month and which give less good surgical results and tend to cure themselves (Barrington-Ward).

Paterson, D, Dobbs, R, and Barrington-Ward, L (1941) *Proc R Soc Med*, 35, 49

PYOMYOSITIS, TROPICAL

TREATMENT

Sulphonamide compounds, especially uleron in 3-gramme doses for courses lasting from 10 to 14 days, are indicated.

1337

As it is generally agreed that the commonest causal organism is *Staphylococcus pyogenes aureus*, treatment with sulphapyridine has been attempted and has given satisfactory results. Earle reported 18 cases of tropical pyomyositis which were successfully treated with sulphapyridine, 2 grammes daily for 5 days. In no case was incision necessary. In 2 cases toxic effects from the drug developed. Both patients complained of epigastric pain and discomfort but it was not necessary to discontinue the use of the drug for such mild reactions. All the cases were complicated by syphilis, malaria, ankylostomiasis, or avitaminosis, sometimes two or more of these conditions were present. The sulphonamide drugs had no effect upon gummatous syphilitic lesions.

Earle, K V (1939) *Trans R Soc trop Med Hyg*, 33, 169

RADIOLOGY IN DIAGNOSIS AND TREATMENT

SYSTEMATIC RADIO-DIAGNOSIS

Alimentary tract

Gall-bladder

As a substitute for iodophthaleinum (sodium tetraiodophenolphthalein) in examination of the gall-bladder, pheniodol (hydroxy-iodo-phenyl-phenyl-propionic acid) is to be recommended.

1342

Circulatory system

Robb and Steinberg^{1, 2} have developed a technique by which the detailed structure of the heart and blood vessels can be visualized. Their method consists in rapid peripheral intravenous injection of a sufficient quantity of radio-opaque solution (70 per cent diodrast) to make the interior of the heart opaque to X-rays during the first circulation, at which time radiographs are made. The length of time between injection of the diodrast and its arrival in the various parts of the cardiovascular system should be measured in each patient, as a preliminary. After the beginning of the injection in an average normal person the superior vena cava and its tributaries and the right auricle are opaque in $1\frac{1}{2}$ seconds, the right ventricle and the pulmonary arterial tree in 3 seconds, the pulmonary veins and the left auricle in 6-8 seconds, and the left ventricle and the thoracic aorta in 8-10 seconds. The optimal degree of rotation for the oblique views should also be determined in each case. The structures visualized when this technique is used include the superior vena cava and its tributaries, the four chambers of the heart and their walls, the ventricular septum, the pulmonary and aortic valves and sinuses and the cusps of the aortic valves, the entire pulmonary circulation, the entire thoracic aorta and its wall, including the sinuses, and the innominate, the left common carotid, and the left subclavian branches from the arch, and the abdominal aorta, the tricuspid valve, and the trabeculae. The exact visualization and measurement of these various structures obviate the use of arbitrary measurements of the cardiac shadow which have no anatomic counterpart.

Mass radiography

Mass (miniature screen) radiography is being used to a large extent in the detection of tuberculosis in recruits for the Forces. The incidence of pulmonary tuberculosis in 100,000 persons so far examined has been found to be 0.3 per cent. The method may eventually prove to be valuable in the control of tuberculosis, but the medical advisory committee appointed by the Minister of Labour and National Service concludes that the procedure is at present impracticable as a routine in the examination of all recruits owing to problems of centralization, and to the limited supply of expert radiologists. The results obtained by modern methods of fluorography or miniature radiography are sufficiently good to enable an experienced observer to select certain patients for more extensive examination by orthodox methods. There is one disturbing element about mass radiography: the patient with the quiescent or old disease which has not given trouble for years may have a certain amount of mental disturbance when he or she is told that a lesion has been discovered, despite assurance given that the disease is no longer active.

Report of Medical Advisory Committee to Minister of Labour and
National Service (1942) Cmd. 6353

Robb, G. P., and Steinberg, I. (1939)¹ *Amer. J. Roentgenol.*, **42**, 14
— — (1939)² *Ann. intern. Med.*, **13**, 12

RAT-BITE FEVER

BACTERIOLOGY AND MORBID ANATOMY

Associated streptothrix infections

- 1344 Since the isolation of a streptothrix, *Str. muris ratti*, by Schottmüller in 1914 from a case of rat-bite fever, many other observers have reported the finding of this organism in human beings bitten by rats and other rodents. Brown and Nunemaker have noted that in the United States of America, *Streptobacillus moniliformis* (*Str. muris ratti*) infection is acquired more often by the bite of rats than is *Spirillum minus* infection. They believe that clinically the two conditions are roughly similar.
- Brown, T. M., and Nunemaker, J. C. (1942) *Johns Hopk. Hosp. Bull.*, **70**, 201

RAYNAUD'S PHENOMENON

TREATMENT

Special

Sympathectomy

- 1345 In young women with true Raynaud's disease, by far the most satisfactory treatment, when symptoms are severe, is sympathectomy, but even this surgical treatment is not always completely successful in getting rid of symptoms in the hands (Johnson). Fothergill, Adson and Allen, in a detailed and careful study, have not confirmed the results of Smithwick and his associates on the sensitivity of the digital arterioles to epinephrine, after post-ganglionic sympathectomy, and it now seems to be very doubtful if this has anything to do with the failure to cure completely Raynaud's disease of the hands by sympathetic denervation. The persistence of Lewis's 'local fault' in the digital vessels would seem still to be the most probable explanation, although regeneration of sympathetic fibres no doubt sometimes takes place.

In older persons in whom Raynaud's syndrome is associated with organic obstruction in the arteries, the results of sympathectomy are less encouraging than they

are in true Raynaud's disease. In these older patients attempts have been made to open up the collateral circulation, and of these attempts the intravenous injections of saline solutions, and more recently of serum, have been followed by temporary improvement (Hayward). Hayward has used 800 cubic centimetres of pooled liquid serum which can be given to patients of any blood group without cross matching, this serum is administered intravenously at a rate of about 10 cubic centimetres a minute, and the only untoward symptoms which have been noticed are temporary lumbar pain, which is common, and rigors, which occur in about 30 per cent of cases. After these injections it has been found that the blood volume is increased temporarily and a temporary improvement is noticed in the peripheral circulation. Further work will be needed, however, before it can be said how long this improvement will last, how often the injections will need to be repeated, and how the results of this method of treatment compare, in the long run, with the use of passive vascular exercises, alternating suction and compression, and intermittent venous occlusion. The treatment of Raynaud's syndrome in these older patients is important, since it is often the first evidence of serious organic arterial disease, and anything which alleviates the early symptoms is likely to slow down the progress of permanent circulatory insufficiency which causes so much discomfort and ends, only too often, in gangrene.

Fatherree, T. J., Adson, A. W., and Allen, E. V. (1940) *Surgery*, 7, 75

Hayward, G. W. (1942) *Brit med J*, 1, 285

Johnson, C. A. (1941) *Surg Gynec Obstet*, 72, 889

RECTUM DISEASES

CARCINOMA

Aetiology

Dukes¹ has analysed 1,000 cases of cancer of the rectum treated by rectal excision, and reaches the following conclusions: (1) Rectal cancer is commoner in men than in women. The average age of onset is earlier in women than in men. (2) At the time of surgical treatment the disease is likely to have spread more extensively in young patients than in the middle-aged or elderly. (3) All regions of the rectum may be affected approximately to the same extent, although probably the incidence decreases slightly on passing from the anus towards the pelvic colon. (4) When surgically removed, most cancers have the form of oval ulcers 2-3 inches in diameter and extending over two or three quadrants of the rectum. (5) When more than one malignant tumour is found this may be due either to multiple primary carcinoma or to secondary tumours resulting from venous extension. Multiple primary carcinoma is especially common in cases of polyposis intestinalis. (6) Histological grading is a useful method of subdividing adenocarcinoma of the rectum because it may give an indication of the extent of local spread. Tumours of high grade malignancy are most often found in young patients. A close relation exists also between the histology of rectal cancer and the extent of lymphatic and venous spread. (7) In about 15 per cent of cases of rectal cancer regarded as operable the growth is found to be still restricted to the rectal wall (A cases). In about 35 per cent the growth has spread by direct continuity into the perirectal fat but has not yet caused lymphatic metastases (B cases). Lymphatic metastases are found approximately in 50 per cent of all cases treated by radical excision (C cases). (8) Evidence of extension of rectal cancer within the lumen of the haemorrhoidal veins can be found in approximately 18 per cent of all operation specimens. (9) Lymphatic metastases are commoner in women than in men and in the young than in the elderly. Metastases rarely occur before the primary growth has spread by direct continuity into the perirectal fat. In most cases exhibiting lymphatic spread only a few glands are affected. Evidence of lymphatic permeation is found in about 15 per cent of all cases, these being mostly growths of high-grade malignancy.

Norbury, from a study of the cases at St Mark's Hospital, London, found that: (1) the average age at the time of surgical treatment was 57 years, (2) the disease was almost twice as common in men as in women, (3) the commonest site was the upper rectum or recto-sigmoidal region, and next to this the ampulla, (4) multiple primary growths are not uncommon, and he strongly recommends that when the abdomen is opened, the whole colon should be quickly examined in order to exclude multiple lesions. With 'familial polyposis' many separate carcinomas may be present at the same time.

Morbid anatomy

Dukes and Bussey review the venous spread of carcinoma of the rectum, the procedure for detection of venous spread by vein dissection and the appearance of the intravascular growth are described. In 667 operation specimens of rectal cancer, carcinoma cells were found in the haemorrhoidal veins in 111 cases, the possibility of venous spread was probably greater than this figure indicated, since in other cases the veins were embedded in growth tissue. The presence of growth within the haemorrhoidal veins indicates the certainty of eventual venous dissemination unless

surgical intervention is made, but is not evidence that metastasis in the lungs or liver has already occurred

Clinical picture

According to Norbury, (1) irregularity of the bowel habit should indicate investigation, (2) haemorrhage may be an early or late symptom, (3) anaemia is not so common as it is with carcinoma of the caecum or right segment of the colon, (4) pain is an untrustworthy symptom and may not be manifest until the growth has involved surrounding nerves the rectum is not endowed with pain sensations, but this does not apply to the anal canal which is highly sensitive, (5) loss of weight is a late sign The operability rate gradually rose with increased knowledge and improved surgical technique to 65 per cent in 1941, in other words, some 35 per cent of cases are found to be inoperable when admitted to hospital Education of the public not to neglect rectal symptoms but to consult the doctor, routine examination of the rectum by the medical practitioner in a general overhaul, have been the means of securing treatment in the early stages of the disease The majority of rectal growths can be felt by the examining finger and until such examination is employed as part of routine investigation, especially in cases with any rectal symptoms, operability will remain at a low figure

Course and prognosis

According to Dukes², who refers to more than 1,000 cases of rectal cancer which were treated by perineal or combined abdomino-perineal excision, for surgical purposes the rectum may be divided into lower third, central ampulla, and upper third, the last including some of the pelvic colon Cancers with lymphatic metastases situated in the ampulla show less favourable operational results than do those in the upper and lower thirds Histologically the growths may be divided into 5 grades of malignancy Extension is both venous and lymphatic, rapidly growing cancers spread through the veins to the liver The number of lymphatic glands affected varies greatly Septic absorption from the ulcerating surface stimulates the proliferation of lymphoid tissue, the cancerous tissue exerts little if any stimulus on the production of new lymphatic glands The greater the number of lymphatic metastases the worse the prognosis, when the glands near the point of ligature of the pedicle are involved the survival rate is poor About 40 per cent of all patients treated by rectal excision were alive after 5 years, and as of the 60 per cent who died at least 10 per cent died from other causes, surgical treatment may be regarded as curing half the number of the cases Recurrence after 5 years is unlikely, and it is rare for an untreated case to survive for that time In cases in which colostomy alone was performed, the operational mortality was 15.6 per cent, more than half the number of patients died within the year, and none survived for 5 years The hospital operability rate amongst cases seen at St Mark's Hospital, London, rose, with the more general adoption of the combined operation, from 51 per cent in 1930 to 71 per cent in 1936

Diagnosis and differential diagnosis

The value of early diagnosis and of biopsy and its reliability for diagnosis of malignancy is emphasized By this means histological grading can be carried out and this may indicate the extent of local spread A close relation exists between the histology of rectal cancer and the extent of lymphatic and venous spread Biopsy grading may thus be helpful in assessing operability Hepatic metastases should negative radical operation, except in certain cases in which a palliative excision is deemed advisable, but Norbury does not regard enlargement of lymphatic glands adjacent to the neoplasm as a contra-indication to operation

Treatment

At St Mark's Hospital statistics have proved the risk of sepsis and peritonitis to be real in the two-stage perineo-abdominal operation, Norbury and his colleagues prefer Gabriel's technique in a one-stage perineo-abdominal excision which statistics show to have a considerably less operative mortality, which in 1939-40 was 7.5 per cent Pre-operative measures include (1) careful preliminary investigations, such as cardiac efficiency, estimation of renal function, haemoglobin percentage, blood grouping, (2) careful preparation of the bowel for several days before operation, (3) spinal anaesthesia with or without gas and oxygen, (4) post-operative blood and saline transfusion by the drip method, (5) great restriction of fluid by the mouth during the first 48 hours in order to lessen the risk of ileus Saline administration is continued until the colostomy has acted and flatus has been passed or good peristalsis is heard Post-operative retention of urine is common in perineal and combined excisions of the rectum It is usually necessary for a catheter to be passed at regular intervals for 5 or 6 days after operation before normal micturition is restored

Radiotherapy

Roberts considers that the value of colostomy in non-obstructive cases of inoperable rectal carcinoma is doubtful, and that X-irradiation provides a means of

REJUVENATION—RHEUMATIC INFECTION, ACUTE
restoring rectal function and permitting an active life for a considerable period without the necessity of colostomy

- Dukes, C E (1940)¹ *J Path Bact*, **50**, 527
— (1944)² *Proc R Soc Med*, **37**, 131
— and Bussey, H J R (1941) *Proc R Soc Med*, **34**, 571
Norbury, L E C (1941) *Hunterian Lecture Carcinoma of the Rectum*

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REJUVENATION

Corrigendum

In Vol X, p 582, 5 lines from foot of page, for 'Doses of 5 to 10 mgm of testosterone propionate weekly by intramuscular injection', read 'Doses of from 10 to 25 milligrams given twice weekly by intramuscular injection'

RETINA DISEASES

DIAGNOSIS

Vital staining of the retina

Sorsby and his co-workers have, for a considerable time, been experimenting with vital staining of the retina as a step towards its use in the diagnosis and assessment of disease of the fundus, especially of the retina

1364

VASCULAR DISEASES

Venous thrombosis

Arterial disease spasm

Retinopathia centralis angiospastica and serosa allergica—Loewenstein reports 4 cases of retinopathia centralis angiospastica and serosa allergica, and discusses their relation to detachment of the retina. The author, from experience of 72 cases, considers that the condition may possibly be of hereditary angioneurotic origin. Another opinion is that the central retinal process is specific, often tuberculous, and that the exudate is infective or inflammatory. Of the 4 cases described, one was an angioneurotic retinopathy of unknown, probably allergic, origin. The second showed exophthalmos and limitation of ocular movements, with submacular or intramacular exudate, and was diagnosed as posterior scleritis. The third showed a central fundus picture similar to the second, in association with a typical tuberculous irido-cyclitis. The fourth had a subconjunctival chemosis, with later a retinal detachment in a myopic eye. The allergic inflammatory reaction, whether tuberculous or not, is always accompanied by a narrowing of the smallest blood vessels with oedema of the surrounding tissue. This spasm of the retinal and choroidal vessels is important in the development of the central retinopathy. Exudatory processes in the choroid and retina cause retinal detachment. In myopic or in senile patients cystic degeneration with exudate may lead to a tear of the retina with progressive detachment.

1367

DETACHMENT

Treatment

Surgical

For the cure of detached retina, there is now more tendency to use indirect ophthalmoscopy with an extremely high candle-power illumination in tracking and localizing the retinal hole. Bipolar surface diathermy is being replaced in many centres by unipolar methods, the amperage being approximately doubled. Probably less stress is now laid on extensive drainage of the subretinal fluid and less reliance is placed on the value of the post-operation position in regard to the drainage of subretinal fluid.

1379

Loewenstein, A (1941) *Brit J Ophthal*, **25**, 369

Sorsby, A (1940) Section 'Vital Staining of the Retina', *Modern Trends in Ophthalmology* (Sorsby, A, and Ridley, F) London

RHEUMATIC INFECTION, ACUTE

AETIOLOGY

Class incidence

Juvenile statistics

The part played by social conditions so far as the causes of juvenile rheumatism are concerned is an outstanding one, and statistics which refer to acute rheumatism and its cardiac manifestations are illustrative of the importance of these factors. In general, the death rate of acute rheumatism is on the decline but it is falling unequally. The prognosis for children under the age of 15 years is not quite so good as it is for those above that age. Morris and Titmuss report that rheumatism is responsible for 10 per cent of all deaths from heart disease and is actually the cause of almost all deaths from heart disease in persons under 40 years of age. Two per cent of all deaths in England and Wales are represented by juvenile rheumatism, of those persons dying between the ages of 5 and 45, 10 per cent die of rheumatism. It is estimated that there are nearly 200,000 cases of rheumatic heart disease in Great

1380

1380

Britain, juvenile rheumatism is therefore one of the most prominent infective diseases at the basis of chronic illness and disablement. Poverty has much to do with the prevalence of the disease. Taking the mortality from rheumatic heart disease as an index of the dangers, it is clear that in persons between the ages of 20 and 35 years the death rate mounts rapidly as the social and economic level becomes lower, there are more deaths in poorer districts than there are in better-class areas, as population becomes more dense so does mortality increase. Low standards of housing, clothing and feeding and general hygiene are therefore to be regarded as the basis of the aetiology of juvenile rheumatism.

With regard to the organism responsible there is not any clear indication of its identity. Certain streptococci have been blamed but the histological changes of rheumatism are not compatible with a purely streptococcal infection. It is quite possible that allergy and virus infection have some influence. It is well known that tonsillitis is often a forerunner of acute rheumatism and neglect of that condition may be of fundamental importance in the subsequent course of the disease. The clinical picture of the undefined but constant rheumatic pains, the mild sore throat and the general debility of the patient is typical. Within 21 days of such premonitory symptoms the full attack of rheumatism is experienced. It seems that removal of the tonsils lessens the severity of an attack of rheumatism and very often the latter shows itself as chorea without carditis. When carditis does exist, the endocardial lesions are produced by infective organisms which reach the heart by the coronary circulation. The controversy with regard to chorea should be settled, chorea may exist without rheumatic symptoms but if a child suffers from chorea rheumatism should be kept vividly in the mind's eye.

DIAGNOSIS

In children

Difficulties to be expected

It is pointed out by Hansen that about one-third of the number of diagnoses in acute rheumatism is wrong. As in other diseases, abdominal pain very often confuses the issue. Diagnosis of appendicitis may be made. The appendix may be removed, but that may be quite justifiable because appendicitis and rheumatic fever can co-exist. Statistics are also available of children being sent to hospital diagnosed as suffering from poliomyelitis, acute osteomyelitis, tuberculosis and so on and in the end the pain in the extremities was found to be due to rheumatism. Kidney lesions and skin rashes, pneumonia and even psychosis have been, among others, false diagnoses arrived at.

Perry confirms the above findings and remarks that typical rheumatic arthritis flits from joint to joint and the joint affected is the only painful joint for the time being. The response of the pain and of the fever to salicylate of sodium is classical.

Hansen, A. E. (1943) *J. Amer. med. Ass.*, **121**, 987.

Morris, J. N., and Titmuss, R. M. (1942) *Lancet*, **2**, 59.

Perry, C. B. (1943) *Practitioner*, **150**, 213.

RICKETS

TREATMENT

Preventive

Massive doses of vitamin D

1383

In the prophylaxis of rickets much good has been done in recent years by giving massive doses of vitamin D. One system of administration adopted by Wolf and Paterson allowed for the giving of 50,000 units of vitamin D to the infant of 4 weeks of age, 50,000 at 2 months and 600,000 units at 3 months. The first two doses were given in liquid form, but the large dose consisted of vitamin D in the form of a powder, and the latter was mixed with cereal food. There is no possibility of overdosing the infant when this method is used.

Wolf, I. J., and Paterson, N. J. (1944) *J. Pediat.*, **24**, 167.

Vol XI SCARLET FEVER

BACTERIOLOGY AND MORBID ANATOMY

Blood picture

1387

The effect of sulphanilamide on the blood in scarlet fever was investigated by French who found little evidence of untoward effect on any of the elements except the polymorphonuclear leucocytes, at all periods, especially in the first week, there was a constant fall in the total leucocyte count, due to reduction of the neutrophils. The usual initial leucocytosis was absent in the untreated cases in 63 per cent, compared with 23 per cent in the cases treated with sulphanilamide.

COMPLICATIONS, SEQUELAE, AND ASSOCIATED DISEASES

Complications

Gangrene

Only 16 cases of gangrene complicating scarlet fever were reported by 1934 and in a dozen only were complete clinical data available. In a female, aged 4 years,

left suppurative otitis media developed on the thirty-fifth day of an attack of scarlet fever of moderate severity, 5 days later there was pain in the left foot which became blue and cold endarteritis was diagnosed and heparin was given. On the forty-fifth day, left mastoiditis was present and the left leg swollen and of a purple hue as far as the malleolus, the arterial pulse could not be detected in the knee or thigh. A culture of *Staphylococcus aureus* was grown from the blood. Sulphonamides, blood transfusions and vitamins were given and the mastoid signs abated. The foot became worse with sloughing of the skin of the outer aspect and exposure of peroneal muscles. On the fifty-sixth day of the disease amputation was performed below the knee well above the line of demarcation and a good recovery followed, although mastoidectomy was required a fortnight later (Breen).

TREATMENT

Prophylaxis

In a comprehensive review of the control of scarlet fever Gordon urged that notification should include doubtful or abortive cases in order to enable public health authorities to trace outbreaks. Period of isolation for those nursed in hospital or private houses should depend on age, severity and presence or absence of complications. Need for hospital treatment should diminish as the size of families becomes less and housing improves. Current practice does not require freedom from haemolytic streptococci before release from isolation, but with improved therapeutics and individual isolation the majority would be free in from 3 to 4 weeks.

Dick and Dick, the discoverers of the causal agent of scarlet fever, suggested as long ago as 1932 that oral administration of scarlet fever toxin in large doses should be employed for special cases, for example for haemophiliacs and subjects abnormally sensitive to toxin and peptone used in its preparation. In 1940 they recorded their findings in 102 subjects immunized with dried toxin made up as 'enteric coated tablets', at intervals from 2 to 8 weeks after taking up to 75,000,000 'skin test' doses. 94.7 per cent were found to be Dick negative, they conclude that although successful for special cases this procedure is not for routine use.

Active immunization

As a result of only limited success with scarlatinal formol toxoid, Veldee, Peck, Franklin and Du Puy prepared a tannic acid-precipitated toxin for use in doses of 750, 3,000 and 10,000 skin test doses given intracutaneously at 2-weekly intervals. The preparation was bland, causing fewer reactions than unaltered toxin and no abscesses. About 85 per cent of immunized subjects were Dick negative when they were tested from one to 2 months later, nearly the same number were negative on retesting from 44 to 48 months afterwards. Great variations were noted in the ease of immunization, some patients being converted after a single dose and others failing to be converted after two complete courses totalling 18,500 skin test doses.

The subsequent incidence of scarlet fever was 1.96 per cent per 1,000 standard population at the ages of from 6 to 9 years, compared with 9.29 amongst a control group.

The severe reactions and inconstant immunization results produced by subcutaneous inoculation of scarlatinal toxin prompted Fisher and Van Gelder to try the intracutaneous route instead. They gave 3 injections at from 2 to 4 weeks' interval, consisting of 12,600 skin test doses, to one group and 5,600 skin test doses to another. They did not find any difference between the two groups and they therefore recommend the smaller dose. Compared with the usual 5-weekly doses given subcutaneously, in which the conversion rate varies from 90 to 95 per cent, they obtained complete immunization, as determined by the Dick response, in 100 per cent of cases. If their results as regards immunization and relative absence of untoward reactions are confirmed, much of the objection to scarlet fever immunization should become invalid.

Specific

Convalescent scarlet fever serum is claimed by Thalmer to be an efficient therapeutic agent in doses of 20–100 cubic centimetres given intravenously. While the antitoxic content is admittedly lower than that of horse immune serums, human serum is regarded as containing more specific antibodies.

Sulphanilamide

Sulphanilamide has been employed in scarlet fever on the grounds chiefly that the organisms responsible for the disease comprise certain strains of the haemolytic streptococci. Early reports, supported by meagre clinical observations, to the effect that sulphanilamide was effective in controlling the disease have been to a considerable extent discounted by later work. It now appears that sulphanilamide therapy does not influence the toxic stage of scarlet fever, that it has not reduced the incidence of complications, and that it is of no value in reducing the carrier state of discharged patients. Its value as a prophylactic in non-immune contacts is still unsettled. Unless further evidence becomes available to the contrary, it must be concluded that sulphanilamide is of little value in scarlet fever.

state, and says that while clean, sutured wounds heal satisfactorily as a rule, there are occasions when they inexplicably break down in spite of the most meticulous care at the operation. In these cases there is usually evidence of a nutritional deficiency affecting the proliferating powers of the cells or the capacity of the mesodermal cells to lay down intercellular substances. The strength of a scar depends upon the intercellular substance laid down by the fibroblasts and the full maturation of this substance. Effective and rapid deposition of collagen is the essential process in scar formation, but this in itself depends on the proliferation of the mesodermal cells. Callus is formed in the same way, the osteoblasts laying down the tissue which matures into bone. It has long been known that wounds heal poorly in scurvy, and an account was given by Anson and Walter in 1748. In his animal experiments Hunt showed that in guinea-pigs a partial deficiency of vitamin C produced a most profound disturbance on the healing of clean wounds. When there is a sufficiency of the vitamin the mesodermal cells build up a mature vascular scar within 14 days. In scurvy the only intercellular material produced is fluid and amorphous. In the intermediate state of subscorvy, when the deficiency is severe, although not clinically evident, the scar matrix remains immature and of poor holding power, although it is produced in adequate amounts. It is not known whether a state of saturation is necessary for the most rapid and effective deposition of collagen, or whether a vitamin content far short of saturation is enough. It may be that the critical level for vitamin C in the formation of collagen is well below saturation point, but this is not conclusive.

TREATMENT

Administration of vitamin C

Hunt states that the short-lived deprivations of the vitamin in an otherwise healthy individual cannot be compared with those of patients chronically ill with long-standing deficiencies. He showed that vitamin C is of the greatest value in wound healing, although not a panacea, and recommends that it should be administered (1) when clean and rapid healing of the wound is particularly desirable, (2) in major abdominal operations, (3) when a hollow viscus has been opened, (4) when post-operative complications are anticipated, (5) when there is evidence of a nutritional deficiency, (6) in all cases of serious injury. Patients for operation should be saturated beforehand.

Anson, G., and Walter, R. (1748) *A Voyage round the World in the Years 1740-44*, p. 241. London.

Hunt, A. H. (1941) *Brit J Surg*, 28, 436.

SENESCENCE AND SENILITY

NORMAL OLD AGE

Generalized atrophy*Hypoplasia of organs*

Korenchevsky points out that there are many factors in the process of aging and that any attempt to explain senescence by a single cause is likely to be unsatisfactory. He therefore summarizes some of his numerous observations on the hypoplasia of organs obtained from 509 normal rats which were employed as controls in endocrinological experiments, and compares them with data obtained from human organs. Rats continue to grow up to the latest age at which they have so far been examined, namely 500 days, but towards the middle or end of the period which was investigated, the increase in actual weight slows down or may even become stationary, this arrest occurs in the liver, kidneys, heart, adrenal glands, thyroid gland, pituitary gland and thymus, with some limitations in the spleen, prostate gland, seminal vesicles and testes. The thymus is exceptional, in that the actual weight increases only up to the period of sexual maturity, after which it gradually atrophies, with reduction in both the actual and the relative weights. An entirely different conclusion is reached when the relative weights of the organs are considered. In the relative weights a distinct 'major involution' (Warthin) of all except the sex organs develops more or less gradually during the whole process of aging, which may occur very early during the first 3 weeks in rats. In man, the highest relative weight of the adrenal glands, thyroid gland, liver, kidneys, spleen and brain exists at birth or in the first 2 years of life. Although hypoplasia must be regarded as a feature of aging, its significance in senescence cannot be defined with certainty, it may be only a physiological adjustment to the slowing of growth, or it may also be, in part, one of the secondary causes of senescence indicating latent wear and tear of the living tissues and resulting, in old age, in true senile atrophy of the organs. In the latter event the relative hypoplasia of organs provides, independently and on a different basis, additional support for Minot's views that the process of aging starts from the first days of life.

Korenchevsky, V. (1942) *J Path Bact*, 54, 13.

Minot, C. S. (1908) *The Problem of Age, Growth and Death*. London.

Warthin, A. S. (1930) *Old Age the Major Involution*. New York.

SEPTICAEMIA AND BACTERIAEMIA**METHODS OF BLOOD CULTURE**

- 1395** Various methods of blood culture and the selection of suitable media have been investigated by Penfold, Goldman and Fairbrother with the purpose of determining the relative value of the various media and of establishing the most satisfactory series for routine investigation. They used two methods: routine blood cultures on patients, and blood cultures inoculated artificially with organisms recently isolated from human patients. Of 160 routine blood cultures 33 gave positive results. The organisms most commonly isolated were *Staphylococcus pyogenes* and *Streptococcus viridans*. Others included the non-haemolytic streptococcus, *Pneumococcus*, *Haemophilus para-influenzae*, *Bacterium coli* (one atypical), *Streptococcus haemolyticus* and *Bacterium typhosum*.

The results of this investigation indicate that for general routine work the following media should be used: solid media—saponin broth with agar, and glucose tryptic broth with agar, Hartley's broth and, when micro-aerophilic or anaerobic organisms are suspected, Robertson's meat medium. The saponin medium compares favourably with all the other media particularly in the isolation of *Strep. viridans*, when this organism was isolated the saponin medium gave positive results in every case and as a rule sooner than did the other media. The glucose tryptic broth gave a lower percentage of positive results than did any of the other media, the reason for recommending it is that on several occasions it gave an early growth of *Staph. pyogenes*, preceding those with other media by from 12 to 48 hours.

SIGNIFICANCE OF POSITIVE BLOOD CULTURES**Sequel to dental extraction**

Elliott has reported on the transient streptococcal bacteraemias which frequently follow extraction of teeth, particularly in cases in which there is severe chronic infection of the gums. In such cases bacteria may gain entrance into the blood stream irrespective of operative procedures, and probably as a result of minor degrees of gum injury such as is produced by biting on a loose tooth. Acute apical infections do not appear to be particularly associated with blood infection of this kind, the focus of infection apparently being effectively walled off by the associated inflammatory reaction. In the production of these post-operative bacteraemias, infection appears to be more important than does trauma since, when infection is marked, very slight degrees of gum injury are sufficient to produce blood stream invasion. Streptococcal bacteraemias were found to occur in 86 per cent of cases of severe gum infection following the mere 'rocking' of teeth, or even of one tooth only. In the complete absence, however, of the type of trauma produced by rocking of a tooth during its extraction, removal may be carried out without producing a heavy bacterial shower in the blood. As a rule these transient bacteraemias produce no permanent ill-effect, but there is some evidence that, in subjects with abnormal heart valves, they may lead to subacute bacterial endocarditis. Prevention of such bacteraemias may be achieved by reduction or elimination of gum infection and by manipulating an infected tooth as little as possible during extraction.

Elliott, S. D. (1939) *Proc. R. Soc. Med.*, **32**, 747.

Penfold, J. B., Goldman, J., and Fairbrother, R. W. (1940) *Lancet*, **1**, 65.

SEX HORMONES**USE OF SEX HORMONES IN TREATMENT OF MENSTRUAL AND CLIMACTERIC DISORDERS****Preparations and standardization of female sex hormones and gonadotrophic hormones**

- 1397** Dodds reviews the advances of sex hormone therapy and gives the scientific names of the substances which are available to the ordinary practitioner. Gonadotrophic hormone, which is derived from pregnant mares' serum, has not yet been obtained pure. Attempts have been made commercially to separate the follicle-stimulating, the luteinizing, the interstitial cell-stimulating and the inhibitory factors, but at present the commercial preparation is not fractionated, it is mainly follicle-stimulating but contains some luteinizing property. Clinically, an important effect is the possible production of ovulation, although the results which have been obtained by different workers show a large proportion of failures. These may be due to an associated deficiency of pituitary gonadotrophins or to anti-hormones.

Dodds, E. C. (1942) *Practitioner*, **148**, 193.

SHOCK AND COLLAPSE**DEFINITIONS AND AETIOLOGY****Surgical shock***Wound shock*

- 1400** *Observations and records*—Grant supplies a memorandum on the observations which are required in cases of wound shock. There is a wide divergence of opinion

on the exact criteria to be considered in the diagnosis of shock. There may be different types of shock, and therefore it is better to avoid the comprehensive term, and to record instead the patient's general state and progress. This procedure is necessarily exacting and can be done only in a few instances by a clinician. The record should contain all the details of the case from first observation until discharge or death. The history and circumstances of the accident should be known as well as the first-aid treatment, including doses of the drugs used. Injuries on admission, together with X-ray and operative findings, must be described. Loss of fluid by haemorrhage, sweat, vomiting, urine and faeces and blistering are important, thirst and nausea must be noted. Observations on the state of the circulation are of primary importance in the condition of shock, and information can be gained from the appearance, the blood pressure, the pulse and the colour of the patient. Blood pressure is regarded at present as being one of the main guides to the general condition, serial readings should be made at intervals. The rate, rhythm and quality of the pulse are important, it is pointed out that the radial pulse may be almost absent when the blood pressure is within normal limits. A rise in rate may indicate increasing general warmth or haemorrhage. The skin colour changes must be remembered, cyanosis is not obvious in artificial light, and pallor may be due partly to dirt. Skin temperature is useful in assessing the peripheral circulatory state. The onset of a rigor is often preceded by or associated with pallor or coldness, sweating also cools the skin. The rectal temperature is the most accurate guide to blood temperature. The depth, regularity and other features of the respirations should be estimated, and abnormal chest signs should be sought for. The handling of the patient and method and time of warming should be recorded, with the resultant effects on the patient's condition. Details of all treatments, with time, dose and method of administration, are most important, and also details of the administration of all fluids. Operative procedures, anaesthesia and progress require to be noted. If a necropsy is made, this also provides evidence. Observations about the general impressions which are gained during the various stages of the illness may be informative in future cases in the light of increasing experience.

HYPOTHESES OF SHOCK

Loss of body fluid

Haemoconcentration accompanying shock is described by Moon as the outward drainage of plasma due to increased permeability of capillary endothelium, resulting in an increase in erythrocytic concentration, circulatory deficiency, capillary dilatation, oedema, blood stasis and fall of blood pressure. Many substances and agents can induce haemoconcentration, including aqueous extracts of normal tissue, peptone, foreign protein, bile, emetine, histamine, poisons and venoms, products of tissue autolysis, intestinal manipulation, circulatory obstruction, anaphylactic shock, allergic pollen reaction, intestinal obstruction, serious infection, burns, trauma and surgical shock. Intravenous injections of substances which cause external wheals, give the syndrome of shock. Haemoconcentration has been observed in cases of haemorrhage (haemodilution) due to war wounds. This provides a distinction between simple haemorrhage and shock. The author attributes haemoconcentration to the production of an unknown substance, not necessarily toxic, from damaged tissues, which affects the general permeability of capillary endothelium. The induction of shock by products of tissue autolysis and the presence of large non-protein nitrogen content of the blood during shock suggest proteolytic products as a possible agent. Experiments done by others to prove that shock after haemorrhage is due to localized fluid loss are unreliable, as falling blood pressure was the sole criterion of shock and anaesthetics alone may effect this. The author, moreover, induced shock in dogs by peritoneal injections of freshly ground muscle, without pain and haemorrhage, only a slight local anaesthetic was used. Shock was produced and a necropsy showed stasis and oedema in remote organs, a post-mortem feature of shock due to burns. This indicates a widespread and not a localized agent. The efficacy of tannic acid is attributed to tissue coagulation which prevents the spread of the agent. Intravenous injections of dyes during experimental shock also show plasma outflow far from the seat of injury. Experimental evidence dismisses sympathetico-adrenal hyperactivity as a cause of haemoconcentration. Failure of the adrenal cortex leads to loss of capillary tone, recoverable by the administration of the hormone. Haemoconcentration is noted in the critical stages of Addison's disease. A compensating mechanism is observed by sympathetic vasoconstriction, splenic discharge and myocardial stimulation, which result in a momentary recovery of blood pressure leaving the rate of flow still deficient. Breakdown of this mechanism is followed by a rapid fall in blood pressure. Haemoconcentration thus gives warning of impending circulatory collapse when blood pressure is still high. The importance of haemoconcentration in infection was demonstrated by post-mortem examinations of influenza patients with full symptoms, no haemoconcentration being revealed in the non-fatal cases—a useful point for prognosis. Cats which are dying from experimental diphtheritic infection have been

kept alive by the perfusion of the heart with defibrinated blood. Thus circulatory collapse is not due to myocardial deficiency, but to fall in blood volume. Attention is drawn to the self-perpetuating cycle of capillary atony which produces anoxia and vice versa, and leads to death. The author emphasizes the practical significance of haemoconcentration and suggests that more attention should be given to the phenomenon.

Discussion of various theories

The severe trauma or toxic injury which gives rise to the acute circulatory failure which comprises the condition of shock has been analysed by Devine. Disturbance of the circulation is not a simple matter, it is a complex which may be regarded as having certain phases. The first of these is the neurogenic phase which includes primary shock and that experienced in spinal anaesthesia or a fainting fit. Secondly, secondary shock, which may be called haematogenic shock, comes on as a result of the reduction of blood volume after haemorrhage. Thirdly there is a vasogenic phase, the effect here being directly upon the blood vessels, namely histamine shock. Lastly there is cardiogenic shock, the failure occurring centrally. With regard to haematogenic shock the cause is in doubt but it is known that because of the reduction of blood volume there is an acute shortage of oxygen in the tissues, here haemoconcentration is typical. A preventive of this is a diet rich in protein and with ample fluids, and Devine would have all soldiers going into battle fed on these lines.

TREATMENT

Cortin

Selye, Dosne, Bassett and Whittaker of Montreal follow up the work of Selye in 1936 on the syndrome of 'the alarm reaction' by a report on the experimental therapeutic value of the adrenal cortex in traumatic shock and allied conditions. The alarm reaction 'represents the somatic expression of the call to arms of the body's defence mechanism', and is characterized by many degenerative lesions and biochemical changes occurring in shock for which the following concise definition is suggested 'a condition of suddenly developing general damage'. The symptom-complex of the alarm reaction is divided into two phases, the first of shock and the second of counter-shock. The period of shock lasts, according to the severity of the injury and to the animal's resistance, from 1 to 36 hours, during which many animals die. It is immediately followed by an entirely different set of symptoms which are the reverse of those in shock. This second phase is that of counter-shock. As adrenalectomized animals do not pass into the second phase, and as in other animals the adrenals are much enlarged, the cells of the cortex showing activity as do also the chromaffin cells of the medulla, it appears that the adrenals, and especially the cortex, play an important part in counter-shock. Further, the greater the enlargement of the adrenals the more extreme is atrophy of the thymus, these two structural changes are phenomena of counter-shock, whereas the first stage, that of shock, may be correlated with relative insufficiency of the adrenal cortex. Experiments on rats dealt with the therapeutic effects of adrenal cortical preparations on shock, cortin (corticosterone) was extremely active in combating traumatic shock, whereas desoxycorticosterone acetate was not. Repeated small doses of cortin were more effective than was a large single dose of the same total amount. Weil, Rose and Browne, also of Montreal, report the results of the treatment of experimental traumatic shock in rabbits by two methods: (1) administration of both cortin (corticosterone) and desoxycorticosterone acetate—mortality rate 19 per cent, (2) administration of desoxycorticosterone acetate—mortality rate 46 per cent. The mortality rate among 58 rabbits in which traumatic shock was induced, but adrenal cortex preparations were not given, was 62 per cent. It is suggested that the administration of adrenal cortical substances before and after operations and in other causes of shock such as injuries, infections and burns, may be clinically important.

Grant and Reeve publish a report of 100 cases of traumatic shock in air-raid and other casualties, not including crush injuries and burns. The cases are classified in tabular form according to the blood pressure on admission, for example raised, normal or low pressure, the latter being subdivided according to the presence of a slow, moderate or rapid pulse rate. The general features of the cases, such as the patient's age, the time since the injury, the type of injury sustained, haemorrhage, survivals and deaths are listed, with the number of cases in the different groups. The series included persons of all ages, from 8 to 72 years, 30 patients being females. About a third were under 30 and a third over 50 years of age. Group (1) included 9 cases, which were of two types, the first comprising patients who were already hypertensive, in such cases the raised pressure may give a false impression and, if the wounds are severe, collapse may follow, but can often be prevented by transfusion. In the second type of hypertensive patient the rise in pressure was a reaction in persons who were previously normal, who were younger and were generally pale, with a pulse rate of 64 to 92. The injuries varied from minor to severe wounds with haemorrhage. All these patients were treated with rest, warmth and morphine, and one had transfusion. All survived operation and there were not any known fatalities.

Group (2) consisted of 28 cases and represented those cases in which the patients, in spite of severe haemorrhage and injury, had normal blood pressure. In the majority the pulse was from 70 to 100. All were treated for shock and only 6 did not receive transfusion, these 6 all survived until discharged from hospital. In 13 cases there was some degree of collapse within 4 hours, and transfusions were given with satisfactory results, in 3 of these cases renewed bleeding necessitated further transfusion. In contrast there were 9 patients who had immediate transfusion although the blood pressure was not low, and whose condition remained satisfactory. Group (3 a) comprised 9 patients, 7 of them over 50 years of age, 5 had internal injuries and there was severe haemorrhage in 6. Five patients did not show any improvement after rest, warmth and morphine, and they then received transfusion, 4 then improved. All underwent operation and one died on the table and one died 5 hours after admission. In group (3 b) there were 27 patients with 15 over 50 years of age. The majority were badly injured. Only one patient was not given transfusion, but he was given fluids per rectum. Fifteen patients did not show any improvement after two or three hours and received transfusion, only one failed to respond and died. Eleven underwent operation, 6 continued satisfactorily, 3 received further transfusion, and 2 died on the table. Nine patients received immediate transfusion, one died shortly after, 6 underwent further transfusion during operation, and one died on the table. In group (3 c) only 3 patients were over 50 years. The injuries were severe in 11 and were internal in 16, with severe blood loss in 22. Initial pulse rates varied from 100 to 200. All the patients received transfusion, 13 were watched first and, of these, 5 did not respond and died before operation, the other 8 underwent operation, but 2 died on the table and 4 had further transfusion. Transfusion was given early in 14 other cases, one patient failed to improve and died, 3 died shortly before operation, 10 underwent operation, 7 then required further transfusion, and 4 patients died.

Devine, H (1942) *Med J Aust*, 2, 19

Grant, R T (1941) *Brit med J*, 2, 332

— and Reeve, E B (1941) *Brit med J*, 2, 293

Moon, V H (1941) *Amer J clin Path*, 11, 361

Selye, H, Dosne, C, Bassett, L, and Whittaker, J (1940) *Canad med Ass J*, 43, 1

Weil, P G, Rose, B, and Browne, J S L (1940) *Canad med Ass J*, 43, 8

SILICOSIS

AETIOLOGY

Industrial processes

Bagassosis

As a result of certain industrial processes one cause of silicosis of comparatively recent origin may be mentioned, namely bagassosis. The dust from broken sugarcane is called *bagasse* and when the fibre is analysed it is found to contain as a rule anything from 5 to 7 per cent of silica. It so happens that up to 1940 *bagasse* was dealt with by a moist process which trapped the dust, for various reasons a new dry process was adopted and this liberates the dust into the atmosphere. As a result of this change certain workmen who were engaged in the process became affected with respiratory disease. The lesions were acutely inflammatory in type, with extreme dyspnoea as the presenting symptom, but there was very little rise in temperature. It is thought that whole *bagasse* contains an antigen soluble in normal saline to which workers who inhale the dust can become sensitized. The early stages of bagassosis may therefore be regarded as allergic reactions. If this is so, the chronic condition might be a form of silicosis, or a pulmonary reaction to cellulose in its crystalline state, or fibrosis which has come on after a state of oedema has been set up by response to the antigen. Whatever end there may be of the philosophy, the practical results of these experiences were that measures were taken to trap the dust and apparently the problem is solved.

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SKIN DISEASES: I—AFFECTIONS DUE TO INSECTS AND ACARINES

PARASITES BREEDING ON HUMAN HOST

Acarus scabiei

The problem of the child with scabies

Scabies has become of so great importance from a public health point of view that in August 1943 it was made compulsorily notifiable in the London district. There is no doubt that it is a disease which is very much concealed by the civil population, it is brought to light very often by the routine examinations of men and women in the Forces. Nevertheless, as Brain states, the diagnosis is often difficult in children and sometimes examination of the mother or father solves the problem. The methods of diagnosis should be most thorough. The folds of skin,

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for example on the wrist and palm, should be well cleansed with Dettol solution, the burrows may thus be rendered more visible. When the burrow has been discovered a little liquor potassae may be used to moisten the tissues and the contents of the burrow may then be scraped out with a scalpel. Microscopical examination will at least show the ovum if it does not show the parent acarus. Urticaria may confuse the issue in the diagnosis of scabies, for it may be superimposed on a scabies lesion and the latter may not be obvious. Another disease which is a handicap to diagnosis is eczema. With regard to the complications of scabies, the commonest is impetigo and as might be expected the treatment of this condition is not of any value unless the underlying scabies is vigorously dealt with. Brain recommends a hot bath with thorough soaping, then the skin is rinsed and dried and an insecticide is applied all over the body. An infected infant should be powdered from head to foot but in older children the head may be left untreated. Benzyl benzoate emulsion of the National War Formulary appears to be the most satisfactory insecticide, this is applied with a flat brush. Thereafter the patient is exposed to warmth in a room until the whole skin is dry, then clean clothes are put on. The second instalment of the treatment is given 8 days later unless there has been any intolerance of the drug. Infected clothing and bedclothes must be dealt with.

Brain, R. T. (1943) *Practitioner*, 150, 231

SKIN DISEASES. III.—LOCALLY INOCULATED INFECTIONS

Corrigendum

In Vol. XI, p. 183, 11th line of paragraph 1, substitute '*Erysipelothrix muriseptica*' for '*Erysipelothrix (B. supestifer)*'

SKIN DISEASES. V.—TUMOURS

MALIGNANT TUMOURS

Derived from superficial layers of epithelium

Precanceroses

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Pseudo-epitheliomatous hyperplasia—Winer gives an account of White and Weidman's classification of the types of pseudo-epitheliomatous hyperplasia which is divided into three grades, as follows: (1) The mildest, acanthosis only; (2) A high degree of acanthosis and irregular epidermal pegs; also a rupture of the basement membrane at the epidermal cutis junction in places where the cells assumed embryonal characteristics with or without pearl formations; (3) Distinct epithelioma microscopically but not clinically. The subsequent history revealed that the lesions healed spontaneously and the patients did not show metastases and cachexia.

Of 62 patients with chronic ulcers of leg which clinically were not epitheliomatous, 11 had pseudo-epitheliomatous hyperplasia. According to White and Weidman's classification 7 were in grade 1, 2 were in grade 2 and 2 in grade 3.

Of 12 patients with tertiary syphilitic ulcers, 6 were in grade 1, 4 were in grade 2, and of 4 patients with blastomycosis, 2 were in grade 1, one was in grade 2 and one was in grade 3.

Squamous-celled carcinoma

Ulceration—Wilson attempts to correlate the rate of ulceration in 1,265 cases of epithelioma of the lip and skin with factors such as the grade of malignancy of the lesion, the type of previous treatment given if any, the site of lesion and the age of the patient. In cases of squamous-celled carcinoma the rate of ulceration was found to be directly proportionate to the grade of malignancy, except with lesions of grade IV which were found to ulcerate at a rate between those of grades I and II. Previously treated epitheliomatous lesions were found to ulcerate more rapidly than those which were not treated, in recurrent cases the rate of ulceration was most rapid in growths which had not been previously treated with salves and pastes. In general, the rate of ulceration was found to be more rapid in persons over 56 years.

Treatment—Warren, Simmons and Rea report the results of treatment in a consecutive series of cases of cutaneous carcinoma which were diagnosed clinically without biopsy. Of 829 cases of carcinoma of the skin which were not verified by biopsy, 84 per cent were observed for 5 years. There were 57 per cent 3-year cures and 48 per cent 5-year cures of all tumour cases treated. If patients lost and dead of intercurrent disease are counted as cures, the 5-year cures would be 84 per cent, if they are entirely excluded, the percentage would be 76. Recurrences occurred in 13 per cent of cases which showed primary healing and which were observed over a period of one year or more. Primary healing occurred in 94 per cent of the lesions observed for one year or more, more than one-quarter of the number of deaths from cutaneous carcinoma occurred after primary healing. Primary healing should not be considered to be a criterion of cure. Failures are due largely to the use of very light filtered radiation applied to the surface in inadequate dosage, X-rays or radium used at a distance, which is the more general practice today, would have given greater depth doses and would probably have given better results.

X-irradiation—Widmann describes a procedure for treating cancer of the skin with low voltage X-rays (75–135 kilovolts). A specific dosage formula is given which admits of a simple effective and universal method according to the thickness or approximate bulk of the lesion, regardless of the size of the surface area, the size being estimated as shallow or large if it is less or greater than 0.5 centimetre elevation above the surrounding normal skin surface. The skin erythema dose (S E D) is considered as representing 500 roentgens, and this arbitrary factor is used to denote a skin unit value so that the total intensity of roentgens will indicate so many multiples of a skin erythema dose for relative and comparative estimations. The technique is an evolution and summation of 10 years' experience at the Philadelphia General Hospital. Much of the material concerned consisted of extensive fungating and inoperable growths, some were 10 to 15 centimetres in diameter. The recuperative properties of tissue during repair are obviously better in small than in large areas affected by any kind of trauma, but the ultimate tissue tolerance of small and large cancers of the skin is shown clinically to be practically identical for similar intensities of long wave-length radiations, because the increased back-scatter and penetration are compensated by the commensurate increased absorption properties of the progressively larger lesions.

Chaoul's method—Hatchette gives an account of the early results in the treatment of cancer of the skin by the method of Chaoul. In treating malignant skin disease, the aim is to destroy a malignant growth entirely, and at the same time to give as little irradiation as possible to the surrounding healthy tissues so that they receive a minimum amount of damage.

Pfahler's method—By Pfahler's 'saturation method' the tissues are irradiated to the limit of normal tissue tolerance (saturation), by either single or multiple doses, in the region of the malignant disease, and the effect is maintained by additional continuous or fractional irradiation over a period which is long enough to destroy all of the malignant cells or to arrest their growth.

Coutard's method—The most recent outstanding contribution to the method of administering irradiation is that advanced by Coutard, in which numerous very small doses of radiation are given to the tissues. With this method of fractional doses the total dose which the tissue can stand without damage is many times greater than the massive dose such as was given in the early days of irradiation therapy. The Chaoul method is not so much a new method of dosage of the tissues, for dosage may be administered according to the massive technique by following Pfahler's saturation method or by the method of Coutard. This, the latest, method of treatment is largely concerned with a new device for the treatment of tissues and the method of its application. By this means, an X-ray tube with a very short distance between the target of the tube and the tissue gives a distribution of X-rays within tissues which is practically identical with the distribution of gamma rays of radium in similar circumstances. The rapid decline in intensity spares the healthy tissues beneath the tumour from receiving a lethal dosage. Seventy-three patients have been treated by this method during a period of 2 years and uniformly good results have been obtained, although sufficient time has not yet elapsed to warrant the formation of any conclusions. It is believed that the impressions obtained after the treatment are of definite value, and that the next few years will see an increase in the number of patients who are treated by this new method. In this group of 73 patients, 126 malignant lesions of the skin were treated. All have remained healed for 2 years, indicating that the Chaoul type of therapy may be as effective as radium and, if time proves such impressions to be correct, it has certain distinct advantages in the saving of time, the simple technique and the ease of protection of the surrounding tissues.

Derived from hair follicles

Rodent ulcer

Schrek and Gates give a detailed analysis of the data on cutaneous tumours of the carcinoma group, from the records of the Collis P. Huntington Memorial Hospital, Boston, and the Pardville Hospital. The investigation includes particularly (1) the similarities and differences between basal-celled and epidermoid carcinomas, (2) the characteristics of value in differential diagnosis, (3) the efficacy of treatment, (4) the value of grading.

In a group of 581 cases, it was noted that the size, not the duration of the tumour, generally prompts patients to seek hospital treatment. The basal-celled tumours develop in a younger age group than do the epidermoid type. Tumours have two types of malignancy, namely innate and clinical. The innate type is the degree of deviation of the tumour from the prototype, the clinical type is the hazard of the tumour to the life and health of the patient. Both types indicate that epidermoid (squamous-celled) carcinoma is three times as malignant as basal-celled carcinoma is. The basal-celled type recurs, however, in as great a percentage of cases as do the squamous-celled growths. The squamous-celled type has a marked preference for the ears, hands and upper part of the face, in this order of frequency. Basal-celled

- 1413 carcinoma predominates on the upper part of the face, nose and ears, the incidence of both types is higher in males than in females, especially on the ears, neoplasms of the scalp, trunk and legs occur somewhat more often in females, 18 per cent of such growths develop in pre-existing scars. Sixteen per cent of squamous-celled growths (epidermoid) metastasize to regional lymphatic glands

SYSTEMIC CONDITIONS

Malignant

Hodgkin's disease

- 1415 Kierland and Montgomery state that typical cutaneous lesions which histologically reveal Dorothy Reed cells are an uncommon cutaneous manifestation of Hodgkin's disease, although some type of cutaneous manifestation, usually a non-specific toxic pruritus, is usually seen in as many as 50 per cent of cases of Hodgkin's disease. Cutaneous manifestations such as severe toxic pruritus, urticarial lesions, exfoliative erythrodermia, nodules, ulcers and sinuses, are associated with Hodgkin's disease in from 25 to 53 per cent of cases. Usually characteristic lesions are the result of extension or metastasis from a primary lesion or from an involved internal organ. Many authors think that mycosis fungoides, Hodgkin's disease and lymphosarcoma, biologically, morphologically and clinically, are variants of the same disease (Baker and Mann, Cole, Goldman, Krueger and Myer, Miller)

Baker, C, and Mann, W N (1939) *Guy's Hosp Rep*, 89, 83
 Cole, H N (1917) *J Amer med Ass*, 69, 341
 Goldman, L B (1940) *J Amer med Ass*, 114, 1611
 Hatchette, S (1941) *New Orleans Med Surg J*, 93, 509
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SMALLPOX

TREATMENT

Symptomatic

Chemotherapy

- 1416 Several papers have recently been published on the treatment of smallpox by chemotherapy (Chari, Cottrell and Knights, Rao and Natarajan, Wilkinson). Although the results were not invariably successful, especially in the cases reported by Rao and Natarajan, they were on the whole remarkably satisfactory and encouraging. According to Wilkinson, who records his observations on 103 cases treated with sulphanilamide, all observers are agreed on the following points: (1) sulphanilamide exerts its influence on the toxic stage of the disease and (2) is of very great value in the treatment of the septic complications so common in the focal stage. Wilkinson's method was to give 1 gramme of sulphanilamide 4-hourly day and night by mouth. The skin lesions were also painted daily with a saturated solution of potassium permanganate. In the case of unvaccinated patients, Chari has combined the giving of liver extract with sulphanilamide preparations and has come to the following conclusions: (1) Liver extract does not abort the disease or do away with the pustular stage. (2) The toxicity of the acute stage is clearly lessened by liver extract. (3) The convalescent stage is lessened by liver extract. (4) In all cases treated with sulphanilamide, and especially with liver extract as well, disfigurement was less than that which occurred in an untreated case.

Chari, N N (1942) *Indian med Gaz*, 77, 91
 Cottrell, J D, and Knights, H T (1943) *J R Army med Corps*, 81, 7
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SPLEEN DISEASES

SPLenic DISEASES

- 1447 In an attempt to centralize cases of obscure splenic enlargement and thus make consistent and continued observations on their pathology, clinical course and treatment, a group of physicians, pathologists and surgeons agreed to pool their interests and to form the Combined Spleen Clinic of the Columbia Medical Centre, New York. The progress which can be made by such teams is well exemplified by the reports which are now available from this clinic. A vast amount of material has been collected and studied, totalling not less than 1,457 cases in 10 years. Many

of the cases fell into the better defined groups of anaemias and leukaemias. The cases which in bygone days might have fallen into the group of splenic anaemias were distributed as follows: Haemolytic jaundice (typical) 43, haemolytic jaundice (atypical) 15, splenomegaly of undetermined origin 47, congestive splenomegaly (Banti's syndrome) 122 (cirrhosis 64, schistosomiasis 11, outside pressure on splenic vein 3, splenic vein thrombosis 8, cavernomatous transformation of portal vein 2, stenosis of portal vein 1, obstructive factor undetermined 33).

Thompson reviews the group consisting of various types of haemolytic jaundice. This group falls into two main sub-groups. The first is congenital haemolytic jaundice, for which the term 'spherocytic jaundice' is suggested by Krumbhaar. This is a chronic disease of long duration and relative mildness. The presenting symptom is chronic variable jaundice, and the outstanding sign is splenomegaly. The peripheral blood contains spherical erythrocytes which are pathognomonic of the disease. The symptoms may appear at any age, the anaemia may be mild or severe, and in the latent cases the blood count may be normal. The blood smear shows cells which have a diameter smaller than the normal but do not show central pallor. Such cells may be detected in wet preparations and their shape may be determined by a micro-manipulator. These spherical cells form only a small proportion of the erythrocytes, and methods of measuring the mean corpuscular volume may therefore be misleading. The mean corpuscular volume method also gives false results when there is a high reticulocytosis, since reticulocytes are often larger than the normal. Haden has shown that the spherical cells alone are responsible for the increased fragility changes. The spherical microcytes are also present in the patient's relatives who have the latent disease.

The results of splenectomy are uniform and prompt. The serum-bilirubin falls to the normal, the erythrocyte count rises, and the patient is restored to the normal in a few weeks. The operation of splenectomy has not any influence on the fragility, which persists as long as 45 years after splenectomy. The second sub-group includes cases in which the presenting symptoms are haemolytic acholuric jaundice with evidence of blood regeneration and splenomegaly. The blood, however, fails to show the spherical cells with the attendant fragility. Some cases of this type seem to run in families, but yet are atypical and are not cured by splenectomy. In this group are included some cases of sarcoma of the spleen, Lederer's type of acute haemolytic anaemia, and some of the acute and subacute haemolytic anaemias which develop after sulphanilamide therapy.

HEPATO-LIENAL FIBROSIS

Fibro-congestive splenomegaly, Banti's syndrome

The concept that the main pathological changes in the spleen are the result of portal venous congestion seems now to be adequately substantiated. The portal venous pressure in cases of fibro-congestive splenomegaly has been measured and has been found to be great, averaging 36 centimetres of saline as against a mean pressure of 19 centimetres in controls. Although in 60 per cent of the cases a recognizable obstructive factor was found in the liver or portal bed, in the remainder no such factor was demonstrated.

In cases in which the obstructive factor is a definite Laennec's cirrhosis, the results of operation are bad. With other types of cirrhosis, particularly that resulting from schistosomiasis, the prognosis after operation is good.

So far, however, a clear case has not been made out to indicate the necessity for, or the benefits achieved by, splenectomy in such cases. If the splenomegaly is secondary to portal congestion and other factors like liver inflammation, it would appear that spectacular results cannot be expected from its removal. There is now a considerable amount of evidence that equally striking results may be achieved as regards survival and the cure of the anaemia by medical measures alone.

RETICULO-ENDOTHELIOSIS OF THE SPLEEN

Reticulo-endothelial system in splenic disease

Reticuloses and reticulo-sarcoma

Classification—A few years ago it was appreciated that there existed a group of disease pictures akin to Hodgkin's disease which were usually labelled by such names as 'atypical Hodgkin's', 'malignant Hodgkin's'. An attempt was made to develop a reasonable classification of this group of diseases which affect the reticular cells of the spleen and lymphatic glands along the following lines (Robb-Smith).

(1) *Reticulosis* is defined as a progressive hyperplasia of reticular tissue with differentiation to one or more cell types. Important subdivisions of this group include (a) lymphoid, myeloid, and monocytic leucoses (leukaemias), (b) storage reticuloses (lipoidoses, Gaucher's disease), (c) fibromyeloid reticulosis (Hodgkin's disease), (d) reticulum-celled and histiocytic reticuloses.

(2) *Reticulo-sarcomas*. This group includes (a) undifferentiated reticulum-celled sarcomas, (b) lymphosarcoma, (c) 'plasmacytoma' (multiple myelomatosis—lymph gland and spleen involvement rare), (d) mixed type (polymorphic reticulo-sarcoma =

1449

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'malignant Hodgkin's') This classification serves a useful purpose in the study of a number of obscure diseases of the reticulo-endothelial system The clinical and pathological pictures of the reticuloses grouped under (a), (b), and (c) above are well recognized Under group (d) Scott and Robb-Smith have recently described a series of cases characterized by fever and wasting, lymphatic gland enlargement, enlargement of spleen and liver, jaundice, purpura and anaemia with leucopenia The cases ran a fatal course and at necropsy there was found to be a systematized hyperplasia of histiocytes in the affected reticulo-endothelial tissues Some of these contained erythrocytes or erythrocyte debris

Skin manifestations—In reporting a case of mycosis fungoides Berman notes that apart from the skin lesions which finally fungate, liver, spleen, and lymphatic glands are frequently involved Mutations into various histological forms are reported, for example to typical Hodgkin's disease (MacCormac) Monocytic leukaemia may begin by involving the skin and may resemble mycosis fungoides The histological lesion of mycosis fungoides is thus non-specific Three distinct histological types are recognized (1) Hodgkin's type, (2) reticulum-celled sarcoma, (3) lymphosarcoma Mycosis fungoides may thus be regarded as a disease of the reticular cells which may be either a reticulosis or a reticulo-sarcoma

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MacCormac, H (1941) *Brit med J*, 2, 645

Robb-Smith, A H T (1938) *J Path Bact*, 47, 457

Scott, R B, and Robb-Smith, A H T (1939) *Lancet*, 2, 194

Thompson, W P (1939) *Bull N Y Acad Med*, 15, 177

SPRUE, TROPICAL

MORBID ANATOMY AND PATHOLOGY

Biochemical considerations

Steatorrhoea

1453

The first essential in the classification of diseases in which steatorrhoea is the main symptom is pathogenic investigation Stannus suggests four main causes of steatorrhoea, these being as follows (1) A chronic condition of insufficiency of the jejunum and ileum with the resulting inefficiency of secretion and absorption which might be expected, (2) defect or absence of the pumping action of the villi as the result of paralysis of the muscularis mucosae, (3) damage to the intramural nervous system (4) blockage of the lymphatic vessels It must be stressed that the above are theoretical and nothing else The changes in the mucous membrane of the bowel are reactions to the enormous bulk of the matter passing through Another difficulty is that there has not yet been established a normal index of the fat-content of the faeces In investigations very often there is no estimation made of the amount of fat that has been ingested Stannus believes that sprue is the result of failure of absorption of fatty acids and cholesterol So far as unsplit neutral fats are concerned these are absorbed normally and any difficulty in absorption is due to increased quantity of fatty acid present and to incomplete emulsification The 'partition' theory of fat absorption postulates one route of absorption for split fats (the portal venous system) and one for unsplit fats (the thoracic duct) Failure of phosphorylation is one of the main elements suggested as being the cause of sprue How this failure occurs is not determined but it might be due to enzyme deficiency with consequent lack of vitamin B₆ and pyridoxin This would also account for the benefits to be obtained by the giving of liver extract in sprue

Stannus, H S (1942) *Trans R Soc trop Med Hyg*, 36, 123

STERILITY

STERILITY IN THE MALE

Examination of semen

Qualitative

1457

More and more emphasis is being placed by seminologists on the quality of the spermatozoa present in a specimen and less and less on the number It is also now realized that the number of spermatozoa present in different specimens of semen from the same male is subject to wide variations Weisman's statistics show that quality and not quantity is the important factor The view previously held that a husband with a count below 60 million was unlikely to become a father is not therefore now taken

Diagnostic testicular biopsy

In the more obscure cases of male sterility or sub-fertility, when other methods have failed to provide a diagnosis great help can be obtained from carrying out a testicular biopsy This can generally be done under local anaesthesia, and without risk to the testicle All that is necessary is to puncture the tunica albuginea after exposure of the testicle The small button of testicular tissue that extrudes is cut off with a pair of iridectomy scissors and examined microscopically This method provides accurate information about the state of the tubules, and is invaluable

Conditions affecting fertility

Infections of the seminiferous tubules

Another possible cause of male infertility which is receiving more attention is the existence of low-grade infections of the seminiferous tubules. When leucocytes are discovered in the semen, cultures should be made and the genital tract should be carefully investigated for the presence of any infective focus. Often nothing wrong will be found with the prostate and vesicles, and when this is the case a blood infection of the tubules must be postulated. There are reasons for believing that the sulphonamides exert a harmful influence on the genital epithelium, and this being so, they cannot be used for the treatment of such infections. For this purpose the use of an old-fashioned herbalist remedy, garlic, has been advocated by Wiesner in a personal communication. This can be used in the form of a decoction and supplemented by garlic taken in salads.

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Failure of spermatogenesis

Treatment—As is usually the case in medical advances the treatment of the more serious forms of male infertility lags behind their diagnosis. No advances have been made in the surgery of stenosis of the genital ducts, but fortunately it has been found that certain cases of occlusion yield to treatment with testosterone. When therefore there are reasons for believing that azoospermia is due to a blockage of the efferent tubules, the patient should be given injections of a microcrystalline suspension of testosterone. The chief advantage of giving testosterone in this form is that crystals are absorbed more slowly than is testosterone in sesame oil. The effect is therefore similar to that obtained by the implantation of a tablet into a muscle, a weekly injection of two cubic centimetres of an appropriate strength of crystals provides a reservoir from which male hormone is being continually absorbed into the blood stream. Successful results of this form of treatment are not uncommonly obtained in cases of azoospermia.

As has been stated already, oligozoospermia is not now looked upon as being as important a cause of infertility as at one time it was. Considerable help may be obtained in deciding whether it is of importance by the use of a Huhner's or a Sum's test. This consists in the examination of the wife's cervical secretions after coitus has taken place. If plentiful and vigorous spermatozoa are found in these secretions treatment of the husband will not be necessary. If no spermatozoa, or only one or two, are present, the conclusion is that either the spermatozoa are at fault or else there exists some factor in the female secretions which is hostile to them. Should efforts to improve the vigour and number of spermatozoa ejaculated by the husband prove to be unsuccessful, artificial insemination may be carried out. This eliminates the dangers which attend the passage of the spermatozoa through the vagina and ensures that the few which exist in the semen pass into the cervical canal. It is unnecessary to add that every effort must be made to synchronize the insemination with the time of ovulation.

Artificial insemination either with the husband's semen or with that of a donor is being more and more used as a remedy for childlessness. The success of it depends partly upon the use of a good technique and partly on the ability to discover the time of ovulation. Folsome, in reviewing insemination, reports that it is successful in 35–44 per cent of cases. It is necessary to point out that in Great Britain, at present, there do not exist any facilities for obtaining suitable semen when that of the husband is either unprocurable or of too poor quality. Not infrequently childlessness is due to an impotent husband who is unable to produce an emission either by sexual intercourse or by masturbation. When this is the case, insemination with his semen is impossible since it is unobtainable.

Folsome, C. E. (1943) *Amer J Obstet Gynec*, **45**, 915

Weisman, A. I. (1943) *Urol cutan Rev*, **47**, 166

STERILIZATION

STERILIZATION OF THE MALE

Corrigendum

In Vol XI, p. 474, in the paragraph entitled *Incision*, for the third and fourth sentences (lines 4 to 8) substitute the following:

This structure is then carefully separated by dissection from the other constituents of the cord, and two clamps are applied to it at least one inch apart. The intervening portion of the vas is then excised, and the divided ends held by the clamps are ligatured with silk.

STOMACH, TUMOURS AND SOME OTHER CONDITIONS

DIVERTICULA OF STOMACH

Clinical picture

Tracey, reviewing findings in 35 cases including 5 of his own, mentions that the pouches are usually near the cardia. In one case there was a diverticulum of the postero-inferior wall of the pylorus, causing obstruction, this condition was not

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observed at two separate X-ray examinations carried out previously although at one an air-bubble was seen, producing an increase in the duodenal arc. Furthermore, although two operations were performed the pouch was not discovered during the course of them. It lay mostly inside the muscularis. The partial gastrectomy performed was a success. In another series (Rivers, Stevens and Kirklin) the symptoms complained of by 4 if not 5 of the patients were due to the diverticulum. As a general rule there are not any symptoms, if they are present they are caused by other lesions.

Treatment

Pouches in the usual situation in the cardia are difficult to remove with safety although surgery is now more successful than it was formerly. Other lesions being excluded, if there is obstruction or uncontrollable ulceration, or if neoplastic tissue is suspected in the pouch, or furthermore if medical treatment has failed, removal may be attempted, always assuming that the patient is a subject fit for operation.

Rivers, A. B., Stevens, G. A., and Kirklin, B. R. (1935) *Surg. Gynec.*

Obstet., 60, 106

Tracey, M. L. (1943) *Gastroenterology*, 1, 518

STRABISMUS

COMITANT (CONCOMITANT) OR NON-PARALYTIC SQUINT

Aetiology

1465

In 1939 Chavasse published fresh material which proved that a fair number of cases of apparently comitant squint in reality start as a paralytic lesion. For example, the external rectus action can be interfered with in a number of ways during the process of birth. Thus the nerve supply may become impaired by involvement of the nucleus of the sixth nerve in one of the many minute interpositive haemorrhages which may occur, or by involvement of the nerve trunk in larger haemorrhages, or in basal fractures, further, the muscle may be put out of action by rupture of its sheath or by haemorrhages into its substance. That something of this kind is not uncommon is demonstrated by the finding of adhesions between the external rectus and the sclera at some operations for the cure of convergent squint. Although recovery seems to occur from the early lesion, the deviation becomes perpetuated in a more or less comitant convergence, which persists after the initial palsy can be no longer demonstrated. The position becomes more complicated when a muscle such as the superior oblique is involved (for example by injury to its pulley) and compensatory spasm is evoked in its antagonizing elevator, namely the inferior oblique of the other eye. Cases of so-called spasm of the inferior oblique are not very rare and are a fruitful source of ocular torticollis. The effect of the lesion becomes evident on adduction of the eye when it is seen to shoot upwards on nearing the end of its movement towards the nose. Other causes suggested for spasm of the inferior oblique include overdevelopment of the muscle or an abnormality of its insertion. Whatever the cause of the lesion its effect can be dealt with satisfactorily by myectomy of the muscle through a conjunctival incision.

Treatment

Treatment of comitant convergent squint

Results of surgical operation—In assessing the success or otherwise of surgical treatment of convergent strabismus the index generally adopted is the amount of deviation which persists. Dunnington and Wheeler in a review of 211 cases were able to divide their patients into three groups (1) those 3 years of age or less, (2) those from 3 to 8 years of age and (3) those over 8 years of age. The operation was a failure in 14.7 per cent, that is to say the original deviation was only half-corrected or there was an overcorrection. There was not any apparent reason for such failures, but it is emphasized that in certain cases more than one operation is necessary. In 43 per cent of the patients the eyes were straight, of the remainder the proportion of undercorrection to overcorrection was roughly 7:2. Overcorrection was commonest in the second age group.

Chavasse, F. B. (1939) *Worth's Squint or the Binocular Reflexes and the Treatment of Strabismus*, 7th ed., London.

Dunnington, J. H., and Wheeler, M. C. (1942) *Arch. Ophthalmol.*, N.Y., 28, 1.

SYPHILIS

BACTERIOLOGY

Staining

1467

Manouélian, by the use of Séguin's modification of the Fontana-Tribondeau method of staining *Spirochaeta pallida*, has established that this organism divides like any other spirochaete, namely transversely, and often so that it is broken up into fragments as small as half a spiral, which he calls spirochaetogenic granules. They are distinguished from debris or artifact by their adherent tags of periplasm which retain to some extent the spiral shape of the parent organism. Such granules are

found chiefly in resolving and old lesions and in lymphatic glands of patients under treatment. In such cases few or no typical *S. pallida* are found, and this fact has led Levaditi to advance the theory that the organism of syphilis has a life history in which it assumes forms quite different from the original spirochaete. Manouelian, however, disclaims any relation between his spirochaetogenic granules and the granules and other forms described by Levaditi.

Resistance

Retention of virulence of S. pallida in the cold

Bloch has found that *S. pallida* retained its virulence for rabbits after being stored for 72 hours at a temperature varying between 3° and 5° C. Consequently he does not think it is safe to rely on cold to render infected blood innocuous.

MORBID ANATOMY AND PATHOLOGY

Laboratory tests

Serum tests

Discrepancies in results of syphilitic serum tests—A good illustration of the wide differences which can occur in the results of tests by what purports to be the same method of a syphilitic serum test was given in a paper by Mahoney and Harrison at the Assembly of Laboratory Directors and Serologists held in 1938 at Hot Springs National Park, Arkansas. The same 34 syphilitic serums tested in 35 laboratories by 'a widely used sero-diagnostic test' gave positive results ranging from 34 fully positive reactions down to 1 positive and 9 doubtful. In another chart the authors showed the differences in results of tests with the same 34 serums in 37 laboratories 'employing test procedures only a few of which conformed to any generally accepted method'. The differences in results were even more striking, at one end of the scale were 9 laboratories which reported from 28 to 34 positive results with the 34 serums, and at the other were 16 which reported from 0 to 9.

The investigations of the committee on evaluation of sero-diagnostic tests for syphilis have supported those of the League of Nations Health Organization and of the English Ministry of Health in showing the constant need for scrupulous care over technique and for periodical overhaul of methods.

Wassermann test—The conception of the syphilitic serum reaction as a true antibody-antigen reaction has led Richardson to exploit the zone phenomena inherent in such reactions for improvement of the Wassermann test. Working on the Harrison-Wyler method as a basis by using in an additional tube a double quantity of serum with a 10-fold–15-fold dilution of the usual emulsion, he has largely eliminated the non-specific doubtful reactions and has made the test much more sensitive. The advance may be gauged by the fact that the Harrison-Wyler method has so far proved to be the most sensitive of any in Great Britain which did not give false positive reactions.

Flocculation tests

The Kahn verification test—The Kahn verification test has attracted considerable attention on account of the expansion of the list of non-syphilitic conditions giving positive serum reactions which has occurred in recent years, as a result of the increase in the practice of making routine serum tests. The above test is based on the view that Kahn reactions due to syphilis reagent are stronger at 37° C. and weaker at 1° C. than at room temperature, whereas reactions due to other reagents, which Kahn terms the 'general biologic type', are stronger at 1° C. Chargin and Rein submitted 1,565 specimens of serum from various sources to Kahn's laboratory for application of this test. The results showed generally that dermatoses, specific fevers and pregnancy tended to produce reactions of the general biologic type much more often than did so-called normal serums, but serums from 268 cases of pinta gave the syphilitic type of reaction. Of 253 specimens from cases which the authors termed 'problem' cases—since nobody had ever been able to determine whether or not they had been infected with syphilis—83 gave the syphilitic type of reaction with this test, and 79 gave the general biologic type of reaction. In the discussion which followed this paper it seemed to be agreed that the verification test did not give complete help in distinguishing the non-syphilitic from the syphilitic reactor in the absence of any history or sign of syphilis, but a reaction of the general biologic type, if repeated, might be regarded as evidence justifying the exclusion of syphilis.

Use of tests in diagnosis and for control of treatment

Serum tests—Lynch, Boynton and Kimball found that, of 263 students who gave negative serum reactions prior to vaccination, 16 per cent gave some reaction afterwards, which was usually doubtful or weakly positive, to one or more of the standard tests for syphilis. In most cases the reactions remained for 2 months but in some they persisted for as long as 4 months.

Thomas and Garrity found that, in 20,000 routine Kahn tests of recruits at a naval station in California, 32 had given what were well proved to be falsely positive reactions. Half the number of the 20,000 were tested 12 days after vaccination, and 26 of the 32 falsely positive reactions occurred in this series. A large proportion of

these were in recruits who had shown accelerated vaccinia. The authors conclude that vaccinia can cause false reactions to syphilitic serum tests and that positive reactions unsupported by history or signs of syphilis in recently vaccinated persons should not be accepted unless they have remained for a number of weeks.

ACQUIRED SYPHILIS

Primary

In children

Smith has collected 125 cases of acquired syphilis in children under 10 years of age. In the Johns Hopkins Hospital, Baltimore, in 17 years, 45 cases of early acquired syphilis were seen in children under 11 years of age and 90 in children from 11 to 15. In the same period the hospital dealt with 1,025 cases of congenital syphilis and 4,487 of early syphilis in adults. In the children the modes of infection were attempted sexual intercourse, 43, kissing, 15, household contact, 14, transfusion, 9, no information, 44. Females were infected twice as often as were males, mainly as a result of attempted sexual intercourse.

Pyrexia in early syphilis

Lemierre has drawn attention to the danger that syphilitic fever in the early stages of the disease may lead to a false diagnosis. The fever may be unaccompanied by other external signs, or there may be other signs which are not exactly characteristic of syphilis. Hardly a year passes in which the Hôpital Claude Bernard does not admit a case of chancre of the tonsil. The fever which commonly accompanies it leads to a suspicion of diphtheria but this can be excluded by easy detachment of the false membrane. A characteristic of value in the diagnosis is that the lesion is unilateral and is accompanied by well marked submaxillary adenopathy together with relative mildness of the subjective signs.

CONGENITAL SYPHILIS

Diagnosis and differential diagnosis

Critical assessment of signs in mother and child

Davis gives the following as criteria on the question whether or not the infant of a syphilitic mother should be treated: (1) If the mother has received adequate treatment, starting before the fifth month of pregnancy, treatment of the infant should be withheld pending the development of manifest signs. (2) The histological examination of the placenta is unreliable, 20 per cent of infants of syphilitic mothers with normal placentas prove to be syphilitic and 12 per cent of infants with positive placentas never develop syphilis. (3) The serum reactions of the cord blood, or of blood from any other part of a new-born infant, are unreliable since they are only a reflex of the condition of the mother's blood. The reactions of the infant's blood are not very reliable before the fourth week except for comparison with those obtained later. If at the end of one month the reactions are more strongly positive than at 2 weeks, the infant has syphilis. If the blood is negative at 2 weeks, it should be tested every 2 weeks up to 4 months of age and after that every 6 months for 2 years. (4) A positive result of a dark-ground examination of scrapings of the inner wall of the umbilical vein indicates syphilis but a negative result means nothing. (5) Radiographs of the long bones, if interpreted by an expert, afford valuable guidance. The characteristic changes are a combination of osteochondritis, osteomyelitis and periostitis. Recent articles, however, have shown that non-syphilitic conditions may simulate these separate findings in X-ray so that the interpretation must be done carefully.

The little finger and the clavicle signs of congenital syphilis

Grafe has investigated a number of cases for the presence of Du Bois's little-finger sign of congenital syphilis. In this, on account of a dystrophy of the middle phalanx of the little finger on one or both sides, this digit is considerably shortened. In the cases seen at the Leipzig University Skin Clinic the sign was found in 138 patients, of whom 60 were certainly congenital syphilitics, 50 were probably so, and 28 showed no sign of congenital syphilis. Prior to this the author had found the sign in 55 out of 100 cases of congenital syphilis and in 60 out of 120 which were probably of this nature. Enlargement of the inner end of the clavicle (sign of Higoumenakis) was found in 55 patients, of whom 45 were certainly or probably congenital syphilitics, 3 showed no sign, and 7 were not further investigated. Grafe is sceptical of the specificity of this sign.

PROGNOSIS

Venereal diseases and life assurance

Harrison, in an article on venereal diseases and life assurance, summarized the results of investigations of 7 groups of authors into the treatment during the earlier stages of their infection of 1,308 cases of cardiovascular syphilis, general paresis, and tabes. The number classed as having been properly treated at first was only 16, and the details of the papers showed that some of these had received no more than 10 injections. The effect of treatment in the early stages in protection against the late effects of syphilis was illustrated by the figures of the Cooperative Clinical

Group, U S A , and by changes in mortality rates for general paresis, tabes, and aneurysm and in mean ages at death which had occurred in England and Wales since 1920. As regards the figures of the Cooperative Clinical Group, these showed that of patients treated with not less than 20 arsphenamine injections, with corresponding heavy metal, those found to have developed late manifestations in an observation period of from 3 to 10 years had 0.6 per cent symptomatic and 2.6 per cent asymptomatic neurosyphilis, and 1.2 per cent positive and 0.2 per cent possible cardiovascular syphilis. In an observation period of from 10 to 20 years the percentages were 1.6 each symptomatic and asymptomatic neurosyphilis, and 0.0 and 4.9 respectively positive and possible cardiovascular syphilis. By a comparison of results of treatment in respect of muco-cutaneous relapses between the schemes of treatment recommended by the Cooperative Clinical Group and those practised in good clinics in Great Britain the author gave reason for belief that the outlook for well-treated cases in this country was at least as good as that represented by the above figures. As regards rates of mortality from late effects, the author showed that from 1921 to 1937 the crude death rates per million in England and Wales had changed as follows. In general paresis it fell in males from 69 to 30, and in females from 14 to 12, in tabes it fell in males from 32 to 24, and in females from 6 to 5, but in aneurysm it rose in males from 44 to 51, and in females from 10 to 25. The author suggested that the explanation of the differences between the changes in the rates for males and those for females was partly that the males, being mostly in the Armed Forces during the war of 1914-18, were better treated during the earlier stages of their infection than were the females (the civil V D treatment arrangements being then only in their infancy) and partly that, after the appearance of signs of a late effect of syphilis, a male is more likely to be treated promptly than is a female. Harrison also showed that in the years 1921-1937 the mean ages at death rose in the case of general paresis in males by 4.49 years to 51.0, and in females by 2.6 years to 50.3, in tabes in males by 4.59 years to 61.1, and in females by 2.05 years to 59.8, in aneurysm in males by 3.83 years to 59.5. On the other hand it fell in females by 2.7 years to 59.3. In the different age periods the steepest falls in mortality from general paralysis of the insane were below the age of 55, and in tabes under 65. The rise in the mortality from aneurysm in males occurred in the age periods after 65, in females it was evident in every age period. Considering that the peak ages of infection are from 20 to 25 and that arsphenamine treatment began to become generalized in Great Britain in 1914, the protective value of modern treatment seems to be manifest in these figures.

TREATMENT

Arsenical compounds

Massive arsenotherapy in early syphilis

Leifer, Chargin and Hyman in 1941 brought up to date their results of the massive arsenotherapy of early syphilis which was begun in 1933, was interrupted until 1938 and has been continued since then. The drug is administered by the intravenous drip-feed method for about 10 hours on each of 5 successive days. Their cases were divided into three series: (1) cases treated with 4 grammes of neoarsphenamine in the 5 days, (2) cases treated with arsenoxide in total doses ranging from 400 milligrams to less than 1,200 milligrams, and (3) cases treated with total doses of 1,200 milligrams (240 milligrams a day). In the neoarsphenamine series the results were the best, 87 per cent of cases being regarded as satisfactory, 7 per cent as unsatisfactory and 4 per cent as 'pending'. The toxic effects had, however, been too severe, and led to the change-over to arsenoxide. The worst results were obtained with arsenoxide given in doses of less than 1,200 milligrams, the satisfactory cases in this series being 79 per cent of 138 subjects and the unsatisfactory cases 18 per cent. Of 99 cases treated with 1,200 milligrams of arsenoxide, 83 per cent were regarded as having given satisfactory results and 8 per cent unsatisfactory. Of the 33 unsatisfactory results in the three series, 24 were in the lower dose arsenoxide series, and most of the 25 infective relapses which occurred in the three series were in this one. Elliot, Baehr, Shaffer, Usher and Lough, a committee of the United States Health Department set up to evaluate the massive dose therapy of early syphilis, have reported on 968 cases of early syphilis treated in different clinics by three methods: (1) slow intravenous drip with arsenoxide on the lines of Chargin and Reim above, (2) rapid intravenous drip in which the daily dose of 240 milligrams was given in from 1 to 3 hours, and (3) administration of the daily dose by one or more injections in small bulk daily. The incidence of toxic effects was great, especially in respect of haemorrhagic encephalopathy. The results in cases which were observed for a sufficient length of time are stated in terms of expected failures per 1,000 cases observed for from 6 months to one year. They were 171 per 1,000 in sero-negative primary cases treated with less than 1,150 milligrams of arsenoxide and 45 per 1,000 in similar cases in which over 1,150 milligrams were given, in sero-positive primary cases the figures on similar lines were 147 and 128, and in secondary cases, 223 and 105, the averages were 180 and 93. In other words, the expectation in cases of

primary and secondary syphilis treated with 1,200 milligrams of arsenoxide by the above method was that 90·7 per cent of the patients would be cured in 5 days

Methods of administration of the arsphenamine preparations

Stability of neoarsphenamine

Probey and Harrison have found that in unstable batches of neoarsphenamine the instability is revealed as clearly by exposure for 4 days at a temperature of 70° C as for 28 days at 56° C. Of batches with a moisture content of 1·5–3·5 per cent, 30 per cent were found to be unstable by this method, but only 8–10 per cent of those with a moisture content of less than 1·5 per cent.

Action of arsphenamine and bismuth compounds *in vitro*

Kast, Peterson and Kolmer found that disodium arsphenamine produced distinct or total loss of motility of virulent *Spirochaeta pallida* in dilutions as high as 1 in 40,960 when in saline and 1 in 20,480 in serum in 15 minutes at room temperature, and in dilutions as high as 1 in 163,840 in 30–60 minutes. Neoarsphenamine worked similarly in dilutions of 1 in 20,480 in saline and 1 in 5,120 in serum for 15 minutes, and at 1 in 163,840 when applied for 30–60 minutes. Mixtures of neoarsphenamine and virulent *S. pallida* in citrated blood in which the dilutions of neoarsphenamine were as high as 1 in 40,960, when injected into rabbits' testicles after standing for 15 minutes at room temperature, failed to infect. Human beings were transfused with 300 cubic centimetres of from 1 in 1,000 to 1 in 3,000 neoarsphenamine and with 300–400 cubic centimetres of 1 in 10,000 disodium arsphenamine, all in citrated blood, without ill effect. The authors recommend therefore that if a transfusion donor is suspect, the citrated blood should have mixed with it neoarsphenamine to a strength of 1 in 10,000 (1 cubic centimetre of a 1 per cent solution per 100 cubic centimetres of blood) and that the mixture stand for 15 minutes at room temperature before being given.

Eagle in previous publications has shown that arsphenamine and bismuth compounds immobilize and kill pathogenic *S. pallida in vitro*, the effect being influenced by concentration, duration of exposure, temperature, and the presence of tissue extractives—the last noticeably inhibiting the action of these drugs. In order to determine the concentrations which would act in the presence of tissue extractives, he mixed the respective drugs with the fluid oozing from an oedematous chancre in a rabbit and allowed them to act for varying periods. In these conditions arsenoxide had a definite antispirechaetal action within 1 to 2 hours at room temperature (25° to 34° C) when in dilutions of from 1 in 1,000,000 to 1 in 4,000,000, arsphenamine, neoarsphenamine, and silver arsphenamine in dilutions of from 1 in 250,000 to 1 in 1,250,000, and two water-soluble compounds of bismuth in dilutions (of bismuth metal) of from 1 in 50,000 to 1 in 225,000. If it is calculated that a dose of 0·4 gramme arsphenamine when administered to an individual of 70 kilograms is diluted in the body to 1 in 100,000, that 0·05 gramme arsenoxide is diluted to 1 in 800,000, and that 0·04 gramme bismuth metal is diluted to 1 in 1,000,000, it will be seen that the concentrations of the arsenical drugs which are reached in the body after injection of therapeutic doses are higher than those found to be effective *in vitro*, and the author suggests that the mode of action of the remedies *in vivo* may be similar to that *in vitro*. As regards bismuth, the longer duration of action and the higher temperature at which it acts in the body may explain the disproportion between the therapeutic dose (but 0·04 gramme is a very low dose for a man of 70 kilograms: the usual weekly dose in Great Britain is 5 or more times as much) and that which is effective *in vitro*. In this connexion the work of Sollmann, Cole, and Henderson indicates that under injections of insoluble compounds of bismuth the concentration of the metal attained in the body varies from 1 in 2,000,000 in the blood to 1 in 30,000 in the kidney. Eagle suggests that even a concentration of 1 in 2,000,000 acting for weeks may be as effective *in vivo* as that found to be effective *in vitro*.

Side-effects of arsphenamine treatment: their prevention and treatment

Jaundice

Aetiology—Jaundice as a complication of the arsenical treatment of syphilis is on the increase, at the same time there is a comparable rise in the number of cases of infective hepatitis. Much work has been done on this subject, and it is apparent that those who have recently undergone a course of treatment are more likely to be affected with jaundice of this type. A patient who has had a course of arsenical treatment may present exactly the same clinical picture as does one who has not had any treatment with arsenic. Marshall mentions five factors which possibly increase the liability to liver damage in syphilis: (1) The existence of a threshold for an arsenical drug. This is suggested by the fact that as a rule changes begin at a definite point in the course of treatment. (2) Syphilis. (3) Environment. Domestic conditions may be all against prevention of complications or they may induce the spread of infection, always provided that the causative factor is an infective agent. (4) Diet. It is suggested that war-time diet, lacking as it does certain constituents which are intrinsic to a sound bodily structure, may cause the liver to be less re-

sistant and thus prepare the ground for hepatitis (5) Sex The proportion of males to females is very great

Pathology—According to Dible and McMichael every case of arsenotherapy jaundice shows one of various forms of hepatitis There is a strong resemblance between the histological picture of the hepatitis which occurs after serum injections and the hepatitis of epidemic hepatitis and arsenotherapy hepatitis A careful histological investigation shows that the lesions are not syphilitic or due to poisoning by arsenobenzol It is more probable that the damage is caused by the same factor which gives rise to serum jaundice or to epidemic hepatitis

Contra-indications to arsphenamine treatment

Intolerance of arsphenamine treatment in pregnancy

Contrary to a common belief that arsphenamine treatment is well tolerated in pregnancy, Ingraham advances evidence that in this condition women are more susceptible to toxic effects of these compounds He cites 7 maternal deaths attributable to neoarsphenamine which have occurred in one locality of Philadelphia since 1931, and a review of side-effects of 6,345 injections given to 733 pregnant women in Philadelphia General Hospital which revealed an incidence of toxic reactions much higher than that which is encountered in routine work He quotes cases from the literature in support of his thesis, and they include 35 deaths, to which he adds 7 out of his own experience The 42 deaths included 27 from haemorrhagic encephalitis, 4 from collapse, 3 from parenchymatous degeneration of the liver, 2 from dermatitis, 1 from eclampsia, 1 from aplastic anaemia, and 4 in which the cause of death was unknown He suggests that the evidence indicates care in initial dosage, and that 'it would possibly be advisable to give more consideration to adequate preparatory heavy metal therapy before commencing active arsenical treatment even though one is confronted with an early infection in late pregnancy' [The last ten words of this quotation suggest that Ingraham has overlooked the evidence that only bismuth passes the placenta to the foetus until practically the end of the pregnancy (Vol XI, p 598), and that therefore if there is a supposition that the foetus has been infected, bismuth is the remedy of choice]

Pyretotherapy

Typhoid H antigen

Antityphoid vaccine of the ordinary type is unduly toxic, and Kulchar and Card have found typhoid H antigen (made by adding to a 24-hour broth culture 0.5 per cent phenol, and filtering) to be much more tolerable The result is that they have been able to apply this form of treatment to patients for whom ordinary antityphoid vaccine would be contra-indicated They used the double-dose method, the 2 injections being given daily at an interval of 2½ hours After giving two single trial doses containing the equivalent of 50,000,000 to 75,000,000 organisms, their further dosage proceeded on the following lines 75/75, 100/100, 125/125, 300/200, 450/350, 700/400, 700/400, 830/300, 1,000/350 and 1,000/350 The temperature usually rose to between 104° F and 106° F and returned to normal in from 6 to 12 hours

Combined with chemotherapy

Simpson, Kendell, and Rose describe their experiences with artificial fever therapy, which dates from 1931, the apparatus employed being the Kettering hypertherm Practically from the outset the authors have combined chemotherapy with the fever, and a great advantage of the latter is that it seems to protect the patient against anaphylactoid symptoms if the arsenical remedy is given at the height of the fever The authors' present system is to give an intramuscular injection of 4 grains of bismuth salicylate at the commencement of the fever sitting, and the arsenical remedy when the temperature has reached 105° F During the period 1937-41 the authors used arsenoxide in a dose of 60 milligrams as the arsenical preparation Usually one or two sittings were given each week up to 12 sittings Their results seem to have been better than could have been expected from chemotherapy alone in ocular syphilis and in sero-positive resistant cases of syphilis, and they have been impressed by the possibilities of combined fever and chemotherapy in eradicating early syphilis

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TAPEWORM INFECTIONS, INTESTINAL

DIPHYLLOBOTHRIUM LATUM

Symptoms

1470

Totterman has described the anaemia which accompanies this infestation as an erythropoiesis in the marrow with normoblasts and a slight shift to the left in the nuclear index of the neutrophils. When the anaemia is hypochromic the number of normoblasts is not raised and generally the eosinophils are slightly increased. But when the anaemia is of the pernicious type the bone marrow shows an increased erythropoiesis with more megaloblasts and premegaloblasts.

Totterman, G (1939) *Acta med scand*, **104**, Suppl

TETANUS

COURSE AND PROGNOSIS

Vol XII

Prognosis

1481

Cole discusses the prognosis of tetanus, based on an analysis of 43 consecutive civil cases in which the patients received approximately the same method of treatment, this consisted essentially of large doses of antitoxin given immediately after diagnosis, usually by the intravenous route. In most cases the dose was a single intravenous injection of 200,000 international units of antitoxin, but in a few mild cases it was reduced to 100,000 I U. The wound was not touched for one hour and then surgical manipulation was limited to the minimum needed to ensure free drainage and for irrigation with hydrogen peroxide.

The prognosis was best between the ages of 5 and 20 years and worst over 60 years. Good general health is very important. Diseases of the heart and lungs increase the risk of terminal pneumonia. The prognosis was better in females than in males, probably because their wounds were slighter and are kept cleaner. The more severe the wound the more severe is the tetanus as a rule, and the amount of deep sepsis is important in determining the prognosis. The prognosis is best in wounds of the lower limb, and wounds on the upper limb and face are most dangerous.

An incubation period of less than 7 days usually indicates a fatal issue, and one of more than 14 days a good prognosis, but an incubation period between 7 and 14 days gives no indication of the prognosis. A better guide to prognosis is given by the length of time which elapses between the first symptom of the disease and the onset of reflex spasms. The appearance of reflex spasms within 48 hours of the onset indicates that a lethal dose has been absorbed. Administration of antitoxin at the earliest possible moment is important, it should be given on suspicion and not delayed until confirmation of the diagnosis. In the absence of a septic wound which is not draining, antitoxin may be discontinued as soon as the reflex spasms cease.

TREATMENT

Prophylactic

Active immunization

Recommendations by the Medical Research Council—Early in 1939 the Medical Research Council arranged for the provision and supply of tetanus antitoxin in the event of war and made recommendations concerning dosage. The prophylactic

TAPEWORM INFECTIONS—THYMUS GLAND DISEASES

dose is 3,000 international units (I U), equivalent to 1,500 American units (A U), and is contained in a volume not exceeding 3 cubic centimetres. During the early part of the 1914-18 war a dose of 500 A U was administered as a routine measure, and the effect on the case-incidence of tetanus was dramatic before the end of 1914, the tendency since then has been to advocate the administration of 1,000 and more recently of 1,500 A U. The dose to be administered for prophylaxis, in case tetanus antitoxin is again required, has accordingly been fixed at 3,000 I U, this can be increased or repeated if necessary. The ampoules of concentrated antitoxin required for the treatment of cases of tetanus contain not less than 20,000 I U in a volume not exceeding 8 cubic centimetres.

The relation of the A U to the I U is 1 : 2, but in order to avoid confusion the strength of tetanus antitoxin is expressed in both units.

Cole, L. (1940) *Lancet*, 1, 164

Medical Research Council's Recommendations (1939) *Lancet*, 1, 839

THYMUS GLAND DISEASES

DISEASES OF THE THYMUS GLAND

Tumours

Associated with myasthenia gravis

Approximately 50 per cent of all necropsies on patients with myasthenia gravis reveal thymic abnormalities, such as benign or malignant tumours, hyperplasia, or persistence. Until the publication of the paper by Blalock, Harvey, Ford and Lilienthal, only 10 cases of myasthenia gravis had been reported in which attempts had been made to influence the course of the disease by surgical intervention, of these, 5 patients died from the operation, one was uninfluenced, 3 showed some improvement and one, from whom a cystic tumour had been removed from the thymic region, showed an early improvement and remained well for 4 years. The series which is reported here differed from those previously described, in that the operation was performed with the deliberate purpose of removing all the thymic tissue by complete exploration of the mediastinum. Poisoning by curare produces a picture similar to that of myasthenia gravis, hence the authors assume that the thymus gland might be concerned in the production of a curare-like substance which affects neuromuscular endings, thus thymectomy would be a rational procedure. They used three methods to determine quantitatively the effect of thymectomy: (1) a study of the degree of weakness (a) on a given dose of prostigmin and (b) without any medication, (2) the effect of intra-arterial injection of a small dose (0.1 to 0.5 milligram) of prostigmin methylsulphate into the brachial artery—normally this results in profound weakness of the hand muscles and numerous fasciculations, whereas in 9 out of 10 patients with myasthenia gravis, using much larger doses (1.5 to 3 milligrams), an increase in strength of the hand muscles was observed, and there were not any fasciculations, (3) Harvey and Masland's electromyographic method for determining the state of neuromuscular circulation.

The authors give technical details of the operation, with the pre-operative and post-operative treatment, and record their results in 6 cases. There was one death, which was possibly due to operating in the presence of an upper respiratory infection, one case showed insignificant improvement, but of the remaining 4 cases the benefit from total thymectomy in 3 was phenomenal and rapid and in one was slower but progressive. In all 6 persistent thymic tissue was found, tumours were not seen but hyperplasia was present in 5 cases.

The results are encouraging and demand that total thymectomy should be seriously considered in the therapy of myasthenia gravis. They support the view that the thymus gland is directly concerned in the pathogenesis of the disease, although the exact part it plays remains a matter of conjecture.

THYMIC HYPERPLASIA

Diagnosis

A new syndrome

Weber and Wohl describe a case of macrogenitosomia believed to be of thymic origin. The patient, a boy aged 14½ years, showed the muscular and external sexual development of a fully developed man. For nine months he had been shaving. Physical and laboratory examinations were negative. X-ray examination disclosed a lobular mass in the superior mediastinum. No abnormality of the pituitary fossa was present. The mass in the superior mediastinum is believed to be either a hypertrophied thymus or a thymic tumour. It is thought that the case may be a new syndrome, namely macrogenitosomia of the 'infant Hercules' type, similar to that sometimes observed in association with adrenal cortical tumours, but in this instance of thymic origin. As macrogenitosomia of the infant Hercules type is seen only in certain cases of adrenal cortical tumour—presumably those in which the bodily soil is favourable—and only in males, probably this syndrome will be found to occur only in males and in those whose bodily constitution is in some way favourable for

the development of that type of macrogenitosomia The authors intend to institute deep X-ray therapy if evidence is observed that the tumour is growing larger
Blalock, A., Harvey, A. M., Ford, F. R., and Lilienthal, J. L., Jun
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Harvey, A. M., and Masland, R. L. (1941) *Johns Hopk Hosp Bull*, 68, 81
Weber, E. P., and Wohl, M. (1944) *Med Pr*, 21, 22

TONSILS DISEASES**ACUTE TONSILLITIS****Treatment*****Sulphonamides***

1484

Chemotherapy is now customary in order to cut short an attack of tonsillitis Sulphanilamide itself should be used, as the infecting organism is nearly always the haemolytic *Streptococcus pyogenes*, and this drug seldom has toxic effects It should, however, be used with discretion, for the disease is ordinarily self-limited and there is some risk of creating a drug-resistant strain of organism If there is any sign of abscess formation chemotherapy is contra-indicated, since the resolution of a quinsy is much delayed by these drugs

REMOVAL OF TONSILS**Indications and contra-indications**

1488

The massacre of children's tonsils which was commonly practised at the time when this kind of opinion was prevalent is nowadays less in vogue, but nevertheless the contra-indications to the operation remain quite as important as do the indications for it, for there are still many parents who hold the superficial view that if the child's tonsils are to be removed the sooner this is done the better In practice the results of the operation on children under 5 years of age, although not uniformly bad, are often disappointing and lead to hypertrophy or recurrence of the adenoids and of the lymphoid tissue elsewhere in the pharynx or on the back of the tongue as a compensatory reaction to the loss of lymphoid tissue, which seems to have a greater physiological activity in the very early years of life than it does later Should such a child show a pronounced enlargement of the cervical lymphatic glands with a reasonable suspicion of tuberculosis, the operation on the tonsils cannot be avoided, for otherwise there is no hope that the glandular infection can be controlled except by a mutilating dissection of the neck at some subsequent date In the absence of some imperative indication of this kind it is better to wait until the child is at least 5 years of age and preferably still older before advising tonsillectomy The history of one or two sore throats is not a sufficient indication If nasal obstruction is troublesome it often suffices in small children to remove the adenoids and leave the tonsils alone The clear nose then diminishes mouth breathing and the consequent liability to tonsillitis If the operation on the tonsils should be needed later, the result is likely to be more satisfactory Why the tonsils should enlarge in some children more than in others is still an unsolved problem to which the key is probably the nutritional one and will be supplied by biochemical research, but unless the hypertrophy is sufficient to cause mechanical obstruction it does not of itself call for ablation but rather for an inquiry into the deficiency to which it appears to be a physiological response Although the operation of tonsillectomy is so commonly performed, in children especially, that it is taken almost as a matter of routine by some parents and by some medical practitioners, it does carry with it, as does every operation however trivial, some risk The risk is not necessarily only of life itself or of an immediate post-operative haemorrhage A disabling otitis media may come on afterwards, lung abscess has occurred, and there are tragic instances of poliomyelitis as an immediate sequel It is important, therefore, if the operation must be undertaken, to choose a suitable time As the principal indication is a history of recurrent sore throats, the time is usually a matter of election, and only the prospect of rapid softening and abscess formation in the cervical glands makes the matter urgent The months during which colds and influenza are rampant are therefore to be avoided if the risk of otitis media is to be reduced to the minimum It seems probable that when poliomyelitis has occurred after the operation the virus may have been already present in the nasopharynx and the wound has opened a path for invasion of the nervous system It is stated that the poliomyelitis is usually of the bulbar type in such cases and this supports the view that spread of the virus takes place through the wound In any case it is an obvious precaution to avoid such operations during and for several months after an outbreak of poliomyelitis in the district, for the disease may not be introduced into the wound from outside but may be stirred into activity in the nasopharynx of a carrier In short, tonsillectomy in children is not to be regarded much in the same way as the shedding of deciduous molars but is to be undertaken for clear indications relative to the probable benefits to be derived

Complications of tonsillectomy***Analysis of two thousand cases***

The complications of tonsillectomy as seen in a series of 2,078 hospital cases are

described by Misra. The operations were done by several surgeons and different methods were used—guillotine or dissection, with either local or general anaesthesia. (1) Haemorrhage was the commonest and most troublesome complication. It occurred in 23 cases—an incidence of 0.8 per cent. It is much more likely to occur in adults than in children. Nineteen of the patients in this series were adults. Fourteen cases were controlled by simple measures such as pressure or application of haemostatics. The remainder required surgical intervention, including in 2 cases ligation of the external carotid artery. (2) Pulmonary complications observed included one case of bronchitis in a child of 6 years of age and one case of lung abscess in a man aged 20 on whom tonsillectomy had been performed under local anaesthesia with the patient in the upright position. Tonsillectomy may light up a quiescent tuberculous lesion in the lung. Two such cases were observed in this series, both in young girls. In one the disease ran a rapidly fatal course, in the other recovery took place. (3) Otitis media may be set up in a previously healthy ear. It was observed in two patients, a child of 8 and a man of 22. In both the attack subsided without operation. (4) General infection with high fever occurred 4 times in this series. Bacteraemia was not detected. All the patients, whose ages ranged from 8 to 25, recovered under treatment with sulphonamides. (5) One case of atrophy of the uvula was observed in a man 20 years of age. The uvula, which had not been injured during the operation, became oedematous on the second post-operative day and subsequently shrivelled up. (6) Change of voice was noted in one case, but an attack of acute post-operative laryngitis was probably responsible rather than was the operation itself. (7) Deep cervical phlegmon occurred once, as the result of perforation of the superior constrictor muscle by the needle used for injecting the local anaesthetic. (8) Surgical emphysema occurred after the guillotine operation in one case. (9) Acute rheumatism developed in one child of 10 years of age who later died of myocarditis, possibly tonsillectomy resulted in a 'flare-up' of a latent rheumatic myocarditis. (10) Habitual dislocation of the jaw, which occurred after tonsillectomy under general anaesthesia in one young woman, was thought to have resulted from rupture of the temporo-mandibular ligaments by over-forcible use of the gag during the operation.

Operative technique

Treatment of bleeding

A modification of the treatment already described in the *Encyclopaedia*, Vol. XII, p. 44, is the application of sulphanilamide to the raw tonsil beds. The local application of sulphanilamide to the large wounds created by the major operations on the pharynx, such as laryngectomy and lateral pharyngotomy, has had a most valuable effect in controlling the wound infections which were the bane of these operations. In the minor operation of tonsillectomy no such dramatic effect can be expected, but the local application of sulphanilamide has a useful function in reducing post-operative oozing and sloughing and in promoting rapid cicatrization.

Misra, R. N. (1943) *J Indian med Ass*, 12, 108.

TOXICOLOGY. I.—HOMICIDAL, SUICIDAL AND ACCIDENTAL POISONING

SYNTHETIC ORGANIC SUBSTANCES

Cyclic ureides and barbituric acid

Treatment

As a result of favourable results obtained in animal tests, picrotoxin has been tried clinically in barbiturate poisoning. Before using this drug it is important to make a certain diagnosis of the cause of the patient's condition, as there is definite evidence that the drug is dangerous in cases of morphine poisoning.

1496

The dose of picrotoxin is 0.5–2 milligrams and there is a very narrow margin of safety. In barbiturate poisoning, however, much higher doses can be used. The drug must be given in divided doses of 3–10 milligrams. Overdosage must be avoided, since a convulsive attack is followed by increased depression. In most of the reported cases the drug had been given intravenously during the first stages of the treatment, at intervals of from 20 minutes to an hour until the patient responded. Since picrotoxin is detoxicated fairly rapidly in the body, the amount present in the blood must be maintained. As the patient improves the intramuscular route may be employed.

INORGANIC AND METALLIC

Mercury

Acute poisoning

The deaths of 4 patients have been reported as a result of the giving of a mercurial diuretic intravenously (Barker, Lindberg and Thomas). It is true that the patients were all in the last stages of disease, with oedema, but 3 had been given the mercurial diuretic (mercupurin, salyrgan) many times before, in fact one patient had had 200 injections. The fourth patient died after the first injection. In one patient mercupurin

1522

1522

set up a severe reaction and later on salyrgan caused fatal symptoms The general reaction to these drugs showed an uncommon pattern—within from 2 to 5 minutes there was extreme irregularity of the heart's action, cyanosis, dyspnoea, unconsciousness and death In another series of cases (Brown, Friedfeld, Kissin, Modell and Sussman), 4 deaths occurred after mercupurin injections had been given, the fatal dose was 2 cubic centimetres and again it was not the first dose Nevertheless it is reported that in 3 out of 4 cases there were either unpleasant effects or distinct reactions after previous injections In a combined experience of many thousands of intravenous injections of mercurial diuretics, the authors state that not one of them has previously observed serious after-effects

Barker, M H, Lindberg, H A, and Thomas, M E (1942) *J Amer med Ass*, 119 1001

Brown, G, Friedfeld, L, Kissin, M, Modell, W, and Sussman, R M (1942) *J Amer med Ass*, 119, 1004

TOXICOLOGY· II —INDUSTRIAL POISONING

TOXIC GASES

Irritant gases

Fluorine and its compounds

1534

Fluorides and the production of magnesium —The industrial hazards involved in the production of magnesium have assumed increased importance because of the demands of war industries for magnesium alloys Williams examines from this point of view the various processes concerned The chief danger arises from the ease with which magnesium and its alloys oxidize at temperatures above their melting points This necessitates the use of special oxidation inhibitors and fluxes which may cause air contamination unless precautions are taken The inhibitors used are sulphuric acid, boric acid, sulphur, soluble fluorides or a combination of these Fluorides are the fluxes usually employed The employees in magnesium foundries are thus liable to be exposed to fluorides, magnesium oxide fumes, sulphur dioxide, chromic acid and carbon tetrachloride, in addition to dust The effects of inhaling metallic magnesium are not known The most important of the contaminants found in magnesium foundries are the fluorides, which occur chiefly in the form of fumes The amount of hydrogen fluoride gas appears to be negligible The soluble fluorides are believed to act as protoplasmic poisons In concentrations exceeding 100 milligrams per 10 cubic metres they have a corrosive action on contact with skin or mucous membranes, shown chiefly by a tingling sensation and running of the nose The effects are rarely serious enough to be reported to the medical officer A filter type respirator prevents these symptoms from appearing Soft paraffin may be inserted into the nose as an added protection If the furnaces and shake-out operation are kept adequately exhausted the amount of fluorides in the atmosphere can be kept within reasonable limits Metal fumes are not present in sufficient concentration to produce 'metal fume fever' Sulphur dioxide concentrations in most foundries are well below 10 parts per million Chrome poisoning occurs rarely and can be prevented by proper ventilation

BENZENE AND ITS HOMOLOGUES

Clinical picture of benzene poisoning

1535

The original conception of chronic benzene poisoning has been found to be an over-simplification based on insufficient human material It was thought that the attack on the bone marrow was always destructive, affecting first the platelets, then the granular leucocytes and finally the erythrocytes The settled belief grew up that a diagnosis of benzene poisoning is not justified unless the blood picture shows an aplastic anaemia associated with a leucopenia, and a relative lymphocytosis, that a leucopenia is more important in diagnosis than is a low erythrocyte count, that cases of benzene poisoning invariably show purpuric manifestations associated with bleeding gums, epistaxis or menorrhagia, that the spleen is never enlarged in these cases, that at autopsy the bone marrow is always in a state of aplasia, that young women are more susceptible than are men to the vapour of benzene, that a concentration of 100 parts per million or less in the air may be considered safe

Although it is true that some advanced cases do show many of these features, we now know that erythrocytosis, leucocytosis, eosinophilia and even leukaemia may be encountered The evidence that chronic exposure to benzene produces leukaemia in human beings is still incomplete, but it is accumulating rapidly and to a volume which commands serious consideration It is best to regard as unsafe any concentration of benzene greater than zero inhaled over a long period The presence in a workshop of the characteristic odour of the solvent is a danger signal Benzene poisoning could best be prevented by abandoning its use as a solvent From medical investigators all over the world comes the plea to use one of the many harmless substitutes Certainly benzene should be used only under the best conditions of ventilation, local or general, with periodical examination of the exposed workers

Chlorinated naphthalene*Acneform reactions and acute yellow atrophy*

Thirteen cases of poisoning by chlorinated naphthalene are described by Collier. The symptoms may take one of two forms, (1) chloracne of the face, especially the cheeks, and (2) acute yellow atrophy. In the series under consideration 12 were of the former and one was of the latter type. The skin lesions are caused by direct contact with dust or fumes of chlorinated naphthalene, and in a typical case include comedones, papules, pustules and sometimes small cysts. Cleanliness is a prime factor in prevention. The acne cases occurred in one department in which for from 3 to 4 months previously technical difficulties had impeded proper exhaust ventilation for the fumes rising from the bath in which chlorinated naphthalene was being melted. In all the cases only the face, excluding forehead and nose, was affected. The thirteenth patient was a woman who had worked for 6 months in the same department, exposed to the fumes from the bath. Four women working with her were unaffected. The case was diagnosed by the doctor as one of catarrhal jaundice and for the first 3 weeks of her illness the patient was treated for this disease, she was then sent to hospital, where she died. At the necropsy the liver was found to weigh only 650 grammes and sections showed acute yellow atrophy.

Collier, E (1943) *Lancet*, 1, 72

Williams, C R (1942) *J industr Hyg*, 24, 277

1537

TRACHOMA**Errata**

In Vol XII, p 218, last paragraph, 1st line, and p 219, top line, for 'lid' read 'lip'—as follows p 218 'The lower lip', and p 219 'The wound in the lip'

EPIDEMIOLOGY**Aetiology**

The disease of trachoma is the result of an infection by a virus akin to the virus which causes psittacosis. It has been claimed that the infecting organism in trachoma belongs to the *Rickettsia* class because some researchers have obtained the Weil-Felix reaction from persons suffering from trachoma, that is to say they have observed a positive agglutination reaction with the *Proteus* group of bacilli. There is not, however, sufficient reason to suppose that there is any arthropod host involved in the evolution of the virus of trachoma.

1545

Incidence and geographical distribution

Diagnosed trachoma is much more prevalent in London now than it was several years ago. This greater prevalence may be attributed to the influx of refugees from Central Europe who are already carriers of the disease or to increased appreciation by ophthalmologists of the diagnostic signs of trachoma.

CLINICAL PICTURE**Initial signs**

The incubation period after infection varies for from 4 to 10 days. Typically the disease begins insidiously but it may begin acutely in the absence of any bacterial infection.

Method of spread of infection

There are a number of persons in Great Britain who exhibit a slight degree of conjunctival inflammation unaccompanied by any serious subjective symptoms. The differentiation of simple conjunctivitis from the specific trachomatous conjunctivitis is difficult. In the absence of any obvious cause the persistence of a chronic conjunctivitis for more than 3 months suggests that further examination by bio-microscopical method should be made in order to detect neovascularization of the cornea (pannus) and that staining of scrapings of the conjunctival epithelium should be done by an expert in this procedure for the detection of virus inclusion bodies.

TREATMENT**Treatment of conjunctiva***Sulphonamides*

The use of copper sulphate in any form may be extremely painful, if it is, this treatment should not be persisted in. Treatment by sulphonamides has been vigorously recommended by ophthalmologists in the United States of America and in some cases, especially when there is some secondary bacterial infection—so common in trachoma—considerable improvement is effected. MacCallan's experience, however, is that virus inclusion bodies persist and thus show that the disease has not been cured. The exhibition of any dosage of a sulphonamide other than full dosage is to be strongly deprecated. All proper precautions should be taken during the treatment and the patient should be in hospital although not necessarily confined to bed.

MacCallan, A F (1943) Personal communication

TRENCH FEVER

AETIOLOGY

- 1548 According to Hurst trench fever has been endemic in Poland for a long time and is still persistent there He gives the incubation period as from 15 to 20 days

TREATMENT

Symptomatic treatment

There is no specific treatment and the sooner the patient is out of hospital the better, since convalescence under good conditions is essential to satisfactory recovery

Hurst, A (1942) *Brit med J*, 2, 318

TRICHINIASIS

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Antigen

Digestive for cysts

- 1549 Lyster finds commercial papain satisfactory in digesting trichinella cysts for diagnosis and as a basis for antigen reactions, 0.1 gramme papain in 313 cubic centimetres of normal saline digests 100 grammes of tissue Digestion is complete in 38 hours

Preparation of antigen

Bozicevich has described the preparation of diagnostic antigen Special care is taken to obtain trichinella larvae from digested infected meat free from protein The dried ground larvae are extracted into neutral 0.85 per cent solution of sodium chloride Preservative is not added, but the vials are subjected to fractional sterilization This antigen shows no loss of titre after 6 months and may be used for both precipitin and intradermal tests

Bozicevich, J (1938) *Publ Hlth Rep Wash*, 53, 2130

Lyster, L. L. (1942) *Canad J comp Med*, 4, 73

TRYPANOSOMIASIS

TREATMENT

Curative

Chemotherapy

- 1553 The therapeutic activity of the diamidines in cases of *gambiense* sleeping sickness has been tested by Lourie and others in West Africa All three diamidines, namely stilbamidine, propamidine and pentamidine, were found to exert powerful trypanocidal action and to produce rapid peripheral sterilization The general conclusion appears to be that a short course consisting of from 1 to 2 milligrams per kilogram of body weight given daily for about 10 days is curative in early cases of the disease There is evidence that propamidine and pentamidine are superior to stilbamidine The action in late cases with profound changes in the cerebrospinal fluid is much inferior to that of tryparsamide

Lourie, E. M. (1942) *Ann Trop Med Parasit*, 36, 113

TUBERCULOSIS

IMMUNITY AND ALLERGY

Factors governing resistance

Tuberculosis and early childhood

- 1554 A primary tuberculous lesion in a child is not so serious as is a tuberculous lesion in an adult, for many years the idea has been abroad that the type of tuberculosis in early childhood was exceptionally virulent, but that idea is being quickly given up (Cameron) The gravity of the situation need not be under-estimated but there is a sound basis for the possibility of satisfactory control Before sensitivity to the tubercle bacillus develops there is a considerable latent period and it is in this period that encapsulation and fibrosis occur, but if sensitivity is established, any attack by the bacillus externally or internally must result in a wider response, which is clearly of an allergic type, it need only be mentioned that the establishment of cutaneous tests for tuberculosis connotes that the condition is an allergic one Allergy is a state of alertness or intensified preparedness for the main attack in conditions in which the less serious preliminary attacks have not succeeded The primary infection may be found in the lung, the eye, the ear, the nose, the throat, the skin or the intestine Intestinal tuberculosis is nearly always caused by milk and is bovine in type Young children should never be given raw milk A renewal of the infection is characterized by a severe reaction which may be fatal and the two danger periods are (1) that which follows immediately after the primary infection and (2) adolescence Meningitis may be expected from the fourth to the sixteenth week after the primary infection occurs Skin tests still hold first place as the most satisfactory index of tuberculous infection and children should be tested at intervals All those who react positively should be examined by X-rays from time to time but it is not necessary to have an X-ray examination carried out on negative reactors

X-rays

Mass radiography

In 1942 the Minister of Labour and National Service presented to the British Parliament a report of his Medical Advisory Committee on mass radiography in the detection of pulmonary tuberculosis among recruits to the Forces. The Committee regards the method as impracticable for application as a routine measure, the most satisfactory alternative being radiological examination after entry into the Forces, when recruits can be concentrated for the purpose at suitable depots. The Navy has examined 100,000 persons in this way and detected about 0.3 per cent of active tuberculosis, the Air Force 12,000 with 0.2 per cent and the Army 4,600 with 0.1 per cent. The civil medical boards which are engaged in the examination of recruits have rejected about 1 per cent with the use of the ordinary clinical and radiological methods of examination. This figure is believed to correspond roughly with that for the general population. Summarizing the position, the report suggests that the number of cases which the medical boards fail to discover by the usual routine methods of examination is between 1 and 2 per thousand. Hall has recorded a survey of mass radiography in two small factories, using a Victor X-ray screening set. In the first, 60 per cent and in the second, 90 per cent of the workers came for examination. Of 575 people examined in the first factory, three were found to be tuberculous. Of 795 examined at the second factory, two were known to have pulmonary tuberculosis and two others were found to have active disease. The workers were of all age groups.

Skin tests

In paediatrics generally and in the examination of child contacts especially the tuberculin reaction is of first importance and there are continued attempts to find an improved technique of testing. The intradermal test (Mantoux) is still regarded as being the most reliable one and it has the advantage of being quantitative to some degree. But it is not altogether convenient for those in general practice. For one thing, the old tuberculin used must be freshly diluted. The use of tuberculin purified protein derivative (P.P.D.) gets over this difficulty. When graded tests are employed it has been the practice to retest with solutions stronger than 1 in 1,000. There is now evidence that concentrated test doses may produce a non-specific reaction. The difference between a specific tuberculin reaction and a non-specific reaction is not altogether clear cut but the latter reaches its peak about twenty-four hours earlier than does a true tuberculin reaction. The tuberculin patch test is gaining in popularity but is not as accurate as the intradermal test nor can it be used quantitatively. There is also a decreasing reliability in older children and adolescents probably because of less penetration of the tuberculin through the outer layers of the skin.

The length of time that tuberculin may remain inactive in certain circumstances is remarkable and may cause unexpected reactions. It is very heat stable and has a tendency to adhere to glassware so that it is practically impossible to remove all of the tuberculin from syringes and it is necessary to keep separate ones for tuberculin testing. For example, if a syringe is used for Schick testing which has previously been used for tuberculin tests, in a subject who is tuberculin-positive a tuberculin reaction may develop. On occasion in persons tested with tuberculin by the intracutaneous method and found to be non-reactors, there has subsequently developed, in some weeks or months, a positive reaction at the site of the previous test injection. This has been attributed to the retention of sufficient active tuberculin in the skin at the site of the injection which gave a reaction when the subject subsequently became infected by chance in the ordinary way.

Cameron, H. C. (1943) *Practitioner*, 150, 291.

Hall, A. S. (1942) *Lancet*, 1, 161.

Report of Medical Advisory Committee to Minister of Labour and National Service (1942) Cmd 6353.

TYPHUS FEVERS

FEVERS OF THE TYPHUS GROUP

Aetiology

The present tendency is to regard all the tick-borne typhus fevers as being so closely related to each other that their causal organisms belong to the same species, although different strains undoubtedly exist. The same remark applies to the various types of mite-borne typhus, but differences of opinion are found among workers on the flea-borne typhus fever. Although in most of the affected localities the latter disease seems to be entirely flea-borne from rats to human beings, some workers believe that lice can become infected by biting patients and then convey the disease to other persons. Such an occurrence must be exceptional, although some experts believe that the virus which is nearly related to that of louse-borne typhus may become modified by transmission through lice and so may give rise to outbreaks of louse-

borne typhus. Such occurrences are believed to have happened in Mexico and in North China. The physician need not concern himself about this debatable point, his working rule must be to handle all cases of fever of the typhus group which occur in persons who harbour lice as if they were louse-borne typhus.

Agglutination tests

Rapid bedside methods of carrying out the agglutination test have been devised, one consists of mixing a droplet of the patient's blood or serum with a suspension of killed *Proteus* OX 19. In positive cases the clumping can be seen with the naked eye or with a pocket lens. The addition of a little methylene blue solution to the suspension facilitates the observation. The same method is applicable to tests made with *Proteus* OXK and OX2. Another method, which is especially intended for making large-scale surveys of areas in which the existence of typhus fever is suspected, is to take droplets of blood on a glass slide, allow them to dry and afterwards add droplets of suspensions of the proteus organisms. When positive results are obtained by either of these methods the standard Weil-Felix reaction should be carried out.

Complement fixation tests and agglutination tests with rickettsial suspensions are now being tried, for both procedures it is claimed that the results are more strictly specific than are those which are obtained by the Weil-Felix reaction. In view of the difficulty which often occurs in distinguishing between louse-borne and tick-borne forms of typhus, there is a real need for a strictly specific test.

The Weil-Felix reaction still holds the field as the standard method of diagnosis of louse-borne and flea-borne typhus, cases have been reported in which normal serums have reacted in titres up to 1-200, but these are readily distinguished because the titre remains constant and does not show the rapid rise and gradual fall which occur in cases of actual infection.

Transmission

Some workers have found evidence that the infection of louse-borne typhus can be conveyed by the faeces of infected lice. It is well known that the dried faeces of infected lice remain virulent for long periods, so that transmission of infection by 'faecal dust' is a possibility, as well as infection through the skin by contact with infected faeces. Disinfection of the skin of the patient by antiseptics is, therefore, advisable, clothing also should be disinfected by heat or by antiseptics rather than by cyanide gas, which cannot be relied on to kill the virus. It is also possible that infection may be conveyed through the skin by contact with the infected blood of the patient, care should be taken to avoid accidental contamination of the skin in making blood examinations.

Transmission by the bite of the infected louse is still regarded as the mode of infection in the vast majority of cases, and louse control is by far the most important method of preventing the spread of the disease.

There is a great deal of evidence that infection may lurk for a long time in infected areas in the form of mild or even non-apparent attacks in children and partially immune persons, the detection of such cases by rapid agglutination tests, such as the 'dry blood' method, is regarded by some German workers as being of great importance.

Prevalence

As is usual in war conditions, the disease has become a serious problem in many parts of Europe, especially in Germany and the eastern occupied countries, but accurate information about the degree of prevalence is lacking.

EPIDEMIC OR LOUSE-BORNE TYPHUS FEVER

Treatment

Preventive

1559

The procedure which holds out the greatest promise of success in peace and war is that of Durand and Giroud. This is based on the discovery that white mice inoculated through the respiratory passages with highly virulent cultures of *Rickettsia prowazekii* develop a massive pneumonia, and their lungs contain enormous numbers of the *Rickettsia* bodies. The emulsified lungs are subjected to differential centrifugalization so as to obtain a fluid which is heavily loaded with the parasites. This fluid is treated with formol and used as a vaccine. The Weil-Felix reaction becomes positive in persons who have been inoculated, and presumably a high degree of protection is established.

NON-EPIDEMIC OR EPIZOOTIC TYPHUS FEVERS

Tick-typhus

Q fever

1560

This disease is related to tick-typhus in being a typhus-like fever conveyed from rodents to man by a tick and caused by a *Rickettsia* body. It was first described by Derrick in 1937 as a new disease occurring in workers in a large meat factory in Brisbane. About 20 cases without any deaths occurred among 800 employees.

UTERUS, DISEASES AND DISORDERS—UVEAL TRACT DISEASES

between 1933 and 1937 The disease lasted from 7 to 24 days, but 1 only out of 9 patients had a definite rash Burnet isolated a filter-passing *Rickettsia* body from experimental monkeys, mice and guinea-pigs The virus, called *R burneti*, is agglutinated by the serum of patients but not by the serum from cases of the other fevers of the typhus group The disease does not protect animals from attacks of the other typhus fevers, and there is no agglutination of *B proteus* OX 19, OX K or OX 2 Bandicoot rats are believed to form the chief animal reservoir of infection in Australia, and a tick, *Haemophysalis humerosa*, is the vector in animals. A virus which is apparently identical was isolated from ticks (*Dermacentor andersoni*) by Davis and Cox in America in 1935, this was called *Rickettsia diaporica* because of its filter-passing properties Only one human case, in a laboratory worker, has been reported from America Q fever does not seem to be of much importance as a human disease but is of great interest as a new form of tick-borne typhus-like fever

Abstracts (1941-2) *Trop Dis Bull*

Cox, H R (1941) *Science*, **94**, 399

Derrick, E H (1937) *Med J Aust*, **2**, 281

Durand, P, and Giroud, P (1940) *C R Acad Sci, Paris*, **210**, 493

UTERUS, DISEASES AND DISORDERS II—DISPLACEMENTS RETROVERSION

Acquired

Treatment

Use of the pelviscope—Harrell describes a method of using the pelviscope designed by himself for the purpose of carrying out uterine suspension without abdominal incision The instrument consists of a tube 1 centimetre in diameter fitted with a trocar by means of which it is passed through the abdominal wall under local or general anaesthesia The trocar is then replaced by a light carried on a stem In performing ventrosuspension the patient is placed in the Trendelenburg position and a horizontal skin incision 1 centimetre long is made 4 centimetres from the midline and 3 centimetres above the symphysis A blunt hook is then used under direct vision to catch the round ligament and draw it into the wound The pelviscope is withdrawn over the hook and the round ligament is sutured to the fascia at the medial side of the wound The procedure is repeated on the other side Skin sutures are unnecessary and the patient can go home on the next day

Harrell, W B (1943) *Amer J Surg NS*, **62**, 149.

1582

UTERUS, DISEASES AND DISORDERS: IV.—TUMOURS

FIBROID TUMOURS

Aetiology

Racial incidence

Fibromyoma of the uterus is commoner in negroes than in white women, the ratio being about 3 3 1 In addition to this, according to Torpin, Pund and Peebles who have reported on 1,741 cases, negroes are affected with much larger tumours Salpingitis occurred as a complication in 16 2 per cent of white women and in 54 per cent of negroes The latter as a rule are affected with necrosis twice as commonly as are white women It is suggested that the reason for the strong predisposition in negro women to fibromyoma is the result of their tendency to develop keloid scars A theory that excess of oestrin leads to fibroid growth is not borne out by a comparison of the endometriums of the two types of uterus—fibroid and non-fibroid One hundred uteruses in the former class and 100 in the latter class were examined and of the fibroid uteruses 20 per cent showed hyperplastic changes in white women and only 10 per cent in negroes So far as the non-fibroid uteruses were concerned the percentages were 15 and 20 respectively

Torpin, R, Pund, E, and Peebles, W J (1942) *Amer J Obstet Gynec*, **44**, 569

1586

UVEAL TRACT DISEASES

DEGENERATIONS

Vascular

Sorsby reviews choroidal angio-sclerosis which is described as a heredo-degenerative disease, and states that apparently three clinical forms have been described (1) 'Central senile areolar choroiditis', in which a moderately regular oval area extends temporally from the disk and engulfs the macula (2) A peripapillary type, with the sclerosis radiating peripherally from the disk in every direction to a variable extent (3) Generalized sclerosis The disease has not been widely recognized as a clinical entity but is not particularly uncommon

Sorsby, A (1939) *Brit J Ophthal*, **23**, 433

1594

VACCINIA AND VACCINATION

VACCINATION

Abnormal results of vaccination

The general eruption

- 1595 When is generalized eruption to be expected in vaccination? Jubb of the Ministry of Health reviews the estimates which have been made, these varying from 1 in every 10,000 vaccinations to 1 in every 900,000 vaccinations. In a survey of the years 1909 to 1941, the incidence is 1 in 96,756 vaccinations. It is pointed out that generalized eruption and post-vaccinal encephalitis when they occur together must constitute a very rare event and the chance of a child's being affected in this way is 1 in many millions, there are only 8 cases on record.

Jubb, A. A. (1943) *Brit med J*, 1, 91

VEIN DISEASES

VARICOSE VEINS

Treatment

- 1596 The treatment of varicose veins depends upon the condition of the vein and the presence of ulceration. When ulceration occurs there are three main factors essential to healing—rest, improvement of blood supply and prevention of infection. In injection of veins by the various methods and with the various remedies now available four reservations must be made. These are (1) too much must not be expected from the drug, (2) the patient must not be promised too much, (3) the surgeon must not be too easily satisfied with the early response, (4) tests of cure must not be neglected. Many different sclerosing solutions have been used, for example 5 per cent sodium morrhuate, 5 per cent sodium oleate, 50 per cent dextrose, 30 per cent sodium salicylate, 10–20 per cent sodium chloride, and quinine hydrochloride 0.26 gramme and urethane 0.13 gramme provided in ampoules containing 2 cubic centimetres of solution in distilled water. The solution most commonly used is 5 per cent sodium morrhuate, 2–7 cubic centimetres being the dose.

PHLEBITIS

Thrombophlebitis

Aetiology

Wright, on the basis of more than 300 cases seen during the last 6 years, discusses the present confused views held about thrombophlebitis and its allied syndromes. It is not generally realized by the medical profession that there may be one, several or many different diseases included under this heading. Of the last 70,000 patients in the New York Postgraduate Hospital, 182, or 0.26 per cent, were the subject of thrombophlebitis. In surgical cases the incidence is from 1.5 to 4 per cent. Among 274 cases analysed the causes recognized were infection 63, varicose veins 51, trauma (a) injury 40, (b) post-operative 52, and unknown 59. Consideration of the classifications clearly showed that there are probably numerous distinct syndromes with individual characteristics as regards causation, physical background, course, and probable prognosis. In some of these syndromes the aetiological factors are quite clear, as in chemical and suppurative phlebitis, in chemical phlebitis the chemical irritation of the intima and other parts of the vein wall causes roughness of the intima and often spasm of the vessel, resulting in stasis with thrombosis, but without any evidence of primary bacterial invasion. There does not appear to be any micro-organism specific, or indeed predominantly numerous, in phlebitis. Attention is directed to the incidence of the relation of epidermophytosis to single and recurrent phlebitis of the feet and legs, this has suggested that the fungous infection may be responsible either directly or by an allergic response, the author and Dunham found that cultures of 15 of such veins were always negative, and that the whole picture is unlike an allergic reaction, and that it is more probable that bacteria, sub-bacterial forms or viruses are admitted through cracks in the skin, produced by the fungus, and track upwards along the veins or lymphatics, this has not been yet proved. All the layers of the veins are usually inflamed and the perivenous lymphatics are involved, so causing oedema (Homans). As a sequel attention is directed to a post-phlebitic neurosis chiefly seen in nervous women.

Treatment

Treatment is described as being in a state of relative chaos, overwhelmed by the number of conflicting methods. Three forms are discussed (1) *Prevention*. This includes the post-operative routine of the application of heat, early movement of muscles, but not to the excess of walking from the operating theatre after laparotomy, avoidance of dehydration and of tight bandages which favour stasis and thrombosis, cure of epidermophytosis of the lower extremities and of any disease of the blood-forming organs. The proper position of the thrombosed limb was formerly elevation, the opinion of Virchow and Aschoff that the commonest site of the origin of thrombosis was the femoral vein and its valve pockets has been contested by Frykholm, in favour of the veins of the calf and adductor muscles.

The results of the raised position of the limb are collapse of the veins and injury to the intima. Logically therefore the usually employed elevation of the limbs is the worst possible position, and he recommends, for both prevention and cure, that for 1–2 hours daily the head of the patient's bed be raised 18 inches, thus filling the veins. In persistent, recurrent and migratory thrombophlebitis abstinence from tobacco seems to be important, in thrombo-angitis approximately 40 per cent of the patients suffer from thrombophlebitis (2) *Conservative treatment* The question of heat or cold applications has raised much controversy, recently local heat has been the more popular, and there are good reasons for this, but the author has seen numerous cases in which heat did not do any good, and a change to a cold application, such as an ice-bag, at once brought about improvement. Probably the greatest source of disagreement is between those who advocate immobilization in bed with only mild movements and those who are in favour of compression bandages with unrestricted activity. For most patients, rest in bed with the leg elevated is the best, the policy of lowering the leg several times a day is prophylactic rather than curative. The use for 2 years of sulphamilamide, sulphapyridine and sulphathiazole has given encouraging clinical results, but the compounds have sometimes failed. In a small series of cases heparin appeared to speed up clinical improvement. The use of leeches has not been beneficial in the author's hands, and hirudin, the active principle of leeches, was disappointing (3) *Radical or operative treatment* Ligature of the vein well above the lesion has been employed to prevent both extension and pulmonary embolism, but it is not a certain preventive. The block of sympathetic ganglion by procaine hydrochloride is based on the fact that vasospasm is often one of the most important factors in the production of pain and disturbance of the venous circulation.

TUMOURS

Haemangiomas*Treatment*

Radium gives good results in a large percentage of cases of superficial haemangioma. It has its greatest value in capillary and cavernous haemangiomas in young infants. Cavernous haemangiomas are best treated by external radium irradiation, combined with interstitial electro-coagulation after several months for the residual growth. External irradiation is by far the best method and gives the most equally diffuse sclerosing effect of any of the sclerosing agents.

Irradiation has given poor results in 'port wine' stains. Solid carbon dioxide is used for very small haemangiomas, for residual patches of haemangioma, for telangiectases around the periphery of a lesion previously treated by irradiation, and also for haemangioma of the scrotum and around the eyelids. Surgical excision, electro-coagulation and desiccation, injection of chemicals, namely quinine and urethane, are not mentioned.

Frykholm, R. (1940) *Surg Gynec Obstet*, **71**, 307

Homans, J. (1939) *Circulatory Diseases of the Extremities*. New York

Wright, I. S. (1941) *Bull N Y Acad Med*, **17**, 348

VITAMINS

HISTORICAL

The concept of vitamins

Dietetic essentials which were not recognized until a few years ago are now well established and have already found important clinical uses, such as nicotinic amide, adermine (vitamin B₆) and vitamin K, knowledge is also accumulating concerning the significance of the still newer vitamins, for example biotin (vitamin H), choline, *p*-aminobenzoic acid and inositol. Perhaps the most striking of such recent work relates to choline, the absence of which produces remarkable changes in the animal organism.

1601

WATER-SOLUBLE VITAMINS

Vitamin B₁ and beri-beri*Vitamin B₁ deficiency*

Assessment of level of nutrition—Shils, Day and McCollum, and also Harper and Deuel, have confirmed the observation of Banerji and Harris that an elevation in pyruvic acid may be used to record the presence of a deficiency of vitamin B₁ in experimental animals. For detecting partial deficiencies in the human subject, as in animals, tests of tolerance to carbohydrate loading were recommended, and have proved of practical use clinically (Elsom, Lukens, Montgomery and Jonas).

1602

Vitamin B₂ complex and the pellagra-preventing (P-P) factor*Other components of B₂ complex*

A review of most recent work on the vitamin B₂ complex has been given by Meiklejohn. Evidence of riboflavin deficiency occurring in men has now been obtained (Sebrell and Butler). Of 18 women who received over a long period a diet similar to that normally associated with pellagra, 13 developed lesions on the face angular

1603

1603

stomatitis and denudation of the mucous membranes of the lips and a scaly desquamation in the nasolabial folds and elsewhere. These lesions responded to administration of synthetic riboflavin but not of nicotinic acid.

Cheilosis (angular stomatitis) has, in the past year or two, come to be considered as the characteristic sign of riboflavin deficiency in man, but, to judge from the clinical observations of Machella, it may be a relatively non-specific lesion, the primary cause sometimes being a deficiency of vitamin B₆, sometimes of nicotinic acid or sometimes even of ascorbic acid.

Nicotinic acid—Pellagra has been very prevalent in Spain since the civil war (Annotation) and, possibly as a result of the present war or perhaps only as a result of better searching, an increased incidence is recorded in Northern Ireland (Deeny). *Assessment of level of nutrition in P-P factor*

Naganna, Giri and Venkatesam, using the method of Harris and Raymond, have confirmed that the urinary excretion of nicotinic acid by patients with pellagra falls to zero and rises to the normal level with cure. As was pointed out by the latter workers, the more precise method of assessing the reserves of nicotinic acid is, however, to administer test doses as is done with tests for other vitamins and so determine the degree of saturation—that is, the number of days before a surplus is excreted at a constant rate in the urine. In the case of nicotinic acid the method is somewhat complicated by the fact that a large proportion of the nicotinic acid (or amide) ingested is excreted as trigonelline, which is itself biologically inert. Thus trigonelline may be derived not only from nicotinic acid but also from ingested trigonelline which is present in certain foods. In an important paper Kodicek and Wang describe a new method for the estimation of trigonelline. In the test-dose procedure which they recommend the patient is kept on a diet free from trigonelline, doses of nicotinic acid amide are administered, and the urinary excretion of both nicotinic acid and of trigonelline is estimated. Under these conditions the amount of trigonelline derived from inactive materials in the diet is negligible and the excretion of nicotinic acid and of trigonelline gives an index of the level of nutrition. In the absence of the controlled, trigonelline-free diet and of test doses, on the other hand, a more satisfactory indication may be obtained from the excretion of nicotinic acid itself.

Vitamin C and scurvy

1604

Vitamin C requirements hypovitaminosis C and its detection

War-time considerations—With the diminished supply of imported fruits, our bodies' reserves of vitamin C are likely to be far lower than they were before the present war, and it is therefore useful to have the authoritative memorandum of the Accessory Food Factors Committee of the Medical Research Council dealing with the preparation and cooking of green vegetables, which gives rules for treatments which are calculated to cause the least loss. In cooking sour fruits a limited amount of alkali (sodium bicarbonate) can safely be added to save sugar (Mapson and Barker).

There is ample evidence that in man, as in animals, sub-clinical deficiency of vitamins produces a variety of somewhat ill defined but none the less real faults in nutrition (Harris^{1, 2}), for vitamin C deficiency these may include sub-optimal growth, diminished resistance to infection, impaired formation of scar tissue and irregularities in the teeth and gums.

Therapeutic uses of vitamin C—Apart from its value in promoting the adequate healing of wounds (Lund and Crandon), there is also evidence that an abundant supply of vitamin C prolongs the life of experimental animals which have been submitted to severe bleeding (Stewart, Learmonth and Pollock) or to low oxygen tensions (Lucas, quoted by Petersen). It may do this by securing a more adequate supply of oxygen to the tissues.

FAT-SOLUBLE VITAMINS

Vitamin D and rickets

Factors influencing rachitogenesis

1605

It has been emphasized (Knudson and Floody) that fat is one of the many factors—others include the acid-base reaction, the calcium-phosphorus ratio, presence of heavy metals, sugars and so forth—which have an effect on the production or healing of rickets. Phytic acid is another such important factor, and to it the rickets-producing action of cereals is attributable. The cause of the deleterious action of the phytic acid seems to be partly that it precipitates calcium in the intestine and partly that it renders calcium un-ionized and thus impedes its absorption (Yang, Harrison and Mellanby). Fortunately, when wheat flour is baked with yeast, an enzyme, phytase, which is present in the dough largely destroys the phytic acid (Widdowson).

Vitamin A

Factors influencing utilization of vitamin A

1606

It is becoming apparent that the efficiency with which vitamin A, or carotene, prevents deficiency disease in animals (and presumably in human beings) varies with

other factors in the diet, that is, the utilization of carotene by the rat depends on the chemical nature of the oil which is administered with it (Sherman), prolonged deficiency of vitamin E causes a secondary deficiency of vitamin A (Davies and Moore), the quantity of food consumed also influences the growth rate with any given intake of vitamin A (Muelder and Kelly)

Assessment of level of nutrition

Yudkin has made a careful reinvestigation of dark adaptation as a means of detecting sub-clinical deficiency of vitamin A. Of 24 subjects who were tested for night blindness, the symptoms in all except 3 improved with vitamin A administration. The method, which is in any case relatively specific, can thus be made completely so by taking as the criterion an improvement or otherwise after administration of vitamin A. Yudkin emphasizes that it may be necessary to give massive doses and that, with smaller doses especially, the cure may be only transient. For any given subject there is a critical low level for the vitamin A in the blood, and below this level dark adaptation is adversely affected, unfortunately, however, there did not appear to be any such standard level applicable to all subjects. Benzedrine or alcohol produced a transient improvement, but the supposed adjuvant action of vitamin C could not be confirmed (Stewart). An alternative procedure, biomicroscopy with the slit lamp (Kruse), has been used by Kruse and his fellow investigators in the course of their impressive surveys on the evaluation of nutritional status (Kruse, Palmer, Schmidt and Wiehl), but Kruse is rightly at pains to point out that the ocular lesion (keratosis) is not the sole, first or most important abnormality 'xerophthalmia is not synonymous with avitaminosis A'.

OTHER VITAMINS

New factors

Enumeration

The 'vitamin B₂ complex' includes, by definition, riboflavin and nicotinamide (pellagra-preventing factor), both of which have already been referred to above, and also adermine (pyridoxin, vitamin B₆) and pantothenic acid (filtrate factor, bios IIA) which have been discussed in recent issues of the *Annual Reports* of the Chemical Society. Other vitamins which have been more recently characterized, and which could logically be classified as belonging to the 'B₂ group', include vitamin H (biotin, bios IIB, co-enzyme R), choline, inositol (bios I) and *p*-amino-benzoic acid (possibly identical with the 'anti-grey-hair factor').

Vitamin K

Vitamin K is believed to be essential for the normal synthesis of prothrombin and may actually be the active component of prothrombin. The presence of bile salts in the intestinal tract is essential for absorption of the vitamin, and any condition which leads to deficiency of bile (for example chronic diarrhoea, intestinal obstruction and surgical short circuits) may lead to deficiency of prothrombin in the blood. The vitamin appears to be produced by various bacteria, including the normal inhabitants of the intestinal canal. It is suggested that abnormalities in the intestinal flora in the new-born may partly account for deficiency of prothrombin leading to haemorrhagic conditions in the new-born.

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WHOOPIING-COUGH

TREATMENT

Symptomatic

1613

The treatment of whooping-cough is notoriously unsatisfactory and this makes it all the more essential that prophylaxis should be adopted. It is very dangerous to new-born infants to expose them to the infection, therefore immediate isolation of the patient should be the rule. Banks recommends that if the patient cannot be moved the infant should be kept covered with muslin and should be given from 10 to 20 cubic centimetres of convalescent serum at 3-weekly intervals. There is no need to keep in bed a child suffering from whooping-cough, the more fresh air he has the better for him, cold winds and draughts should be avoided. The giving of vitamin C, ultra-violet light, pure pertussis vaccines and so on is not likely to be of any great benefit, in fact these forms of treatment appear to be very much over-rated. Mixed vaccines containing *Haemophilus Pfeiffer* and *H. pneumococcus* given at 3-day intervals may, however, protect the patient against broncho-pneumonia. When capillary bronchitis does supervene, sulphathiazole is the best available sulphonamide. Doses of 0.5 gramme 4-hourly for 3 or 4 days should be given daily to infants and then the period should be lengthened to 6 hours for another 5 days. The important point is that as infectivity in whooping-cough rarely persists after the fourth week, it is feasible to release children from isolation even if they are actively coughing and vomiting.

Banks, H S (1943) Personal communication

YELLOW FEVER

TYPES AND THEIR GEOGRAPHICAL DISTRIBUTION

1616

Bugher, Boshell-Manrique, Roca-Garcia and Gilmore have investigated the susceptibility to yellow fever of the marsupials occurring in the Villavicencio-Restopo area of Eastern Colombia since jungle yellow fever was first recognized in 1934. Six species of marsupials were tested, of which *Didephys marsupialis*, the black-eared common opossum, was the most abundant. Multiplication of the virus did not cause any obvious signs of illness in any of the species which were tested, and splenectomy did not produce any striking increase in susceptibility to infection. Protection tests, which were carried out during and after the yellow fever outbreak, showed that the reactions of 16 out of 48 adults and young adults were positive. Such results indicate that the above marsupials must play some part in the complex picture of jungle fever in Colombia.

VIRUS AND VECTORS

Vector

Control of *Aedes*

Satisfactory control of the mosquito, *Aedes aegypti*, has been successful in eliminating yellow fever from urban communities and in preventing outbreaks when infected persons have entered these centres from outside. These measures have, however, failed to prevent the spread of yellow fever in areas in which it is endemic in Africa and in the regions in which jungle yellow fever is prevalent in South America. The problem is much more complex than was originally visualized, but our knowledge has made considerable advances in recent years. In South America infected mosquitoes of one of the species which are the insect vectors of jungle yellow fever have been found in tree-tops. As mosquitoes once infected are known to remain so for the rest of their lives, we have an explanation of the prevalence of yellow fever among wood-cutters and of how the virus may be carried over from one rainy season to the next. It may be that a similar carry over of virus from season to season will be found in Africa. In 1940, for reasons as yet unknown, there was a very large localized epidemic of yellow fever in the Sudan, where actual cases of the disease had never been seen before, although immunity surveys had shown infection to be present. *A. aegypti* was abundant in the region, but so also was *A. taylori* and *A. metallicus*, both of which have been shown to be capable of transmitting the disease. The virus was isolated from cases among the native population, but not from mosquitoes. Previous immunity surveys had also indicated that yellow fever was present in an unrecognized form in certain areas in Uganda. After three years of painstaking work,

during which they discovered two entirely new viruses, Mahaffy and his colleagues have isolated a strain of yellow fever virus from a native in Western Uganda, where selected surveys had indicated the recent appearance of the disease. Two strains of yellow fever virus were also isolated from *A. simpsoni* (the mosquito most prevalent in the area) caught in the same district. It is probable that various species of monkeys help to maintain the infection in forest regions in both Africa and South America. Immune bodies for yellow fever virus have been found on a number of occasions in the blood of monkeys in endemic yellow fever areas in Africa and South America. Recently, Hughes has found that certain individuals of the species *Cercopithecus aethiops centralis* Neuman, one of the most ubiquitous mammals in the East African zone of yellow fever endemicity, are capable of harbouring yellow fever virus in high concentration. These monkeys are migratory and travel in small troops, and so if once infected might distribute infection throughout the range of migration. A great deal more work must be done before it will be possible to determine what part other mosquitoes, mammals and birds play in maintaining the disease in forest and rural areas. The isolation of the virus in Uganda stresses the importance of the eradication of all mosquitoes which are likely to be vectors from the East African ports. It also calls for increased vigilance in examination and spraying of all aircraft passing through these areas to India and the East.

Mosquitoes acting as vectors

Aedes geniculatus has been found by Callot in the Department of Indre-et-Loire and in different parts of Alsace and in Seine-et-Oise. It breeds in rock-holes in which there is water containing rotting vegetable matter. This species has been found to be an efficient vector of yellow fever.

Roubaud, Colas-Belcour and Stefanopoulo have shown that *Aedes geniculatus* can transmit yellow fever by its bite if kept at 30 to 35° C., but when these insects were fed on blood containing yellow fever virus and, after 5 days at 30° C., kept at 20 to 22° C., and then fed on a normal monkey, they produced neither infection nor immunity.

In unravelling the yellow fever mystery in recent work on jungle yellow fever in South America, it has been shown that in wild animals which have been inoculated with yellow fever virus illness is not as a rule produced, but that the virus is present in the circulatory blood which is a condition especially favourable to its spread. Several genera of animals are susceptible. These are as follows: (1) Primates—man and monkeys; (2) Marsupials—opossums of all species; (3) Edentates—anteaters, sloths, armadillos; (4) Rodents—agouti, paca, cabybara and some species of mice. The following generalizations are permissible. Yellow fever is primarily a disease of jungle animals. The classical form involves transmission from man to man by *Aedes aegypti* and is to be regarded as more of a secondary cycle depending largely upon conditions of population concentration and mosquito breeding created by man. Transmission of jungle yellow fever appears to be by jungle mosquitoes from animal to animal. There is not any animal reservoir of virus in the usual sense, as the virus continues to circulate in the blood of susceptible animals for 3 or 4 days only (Review, Rockefeller Foundation, 1940).

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Protection tests

Mouse-protection test

The Yellow Fever Commission does not recommend the mouse-protection test for the diagnosis of yellow fever in doubtful febrile diseases with clinical signs of yellow fever. It is only of real value for making a retrospective diagnosis in a community suffering from an epidemic of uncertain nature.

Galois has given the results of examination of the first 5,000 liver specimens which were obtained in Colombia by means of the viscerotomy. Since 1934, shortly after jungle yellow fever had been shown to exist in the interior of Colombia, 117 viscerotomy posts were established throughout the country. Of these 5,000 specimens, 196 were diagnosed as being positive for yellow fever. In many the diagnosis was confirmed subsequently by full investigations. By this means also epidemics of fatal malaria were brought to light.

TREATMENT

Prophylaxis

Prophylactic vaccination

The most satisfactory means of combating jungle yellow fever or any other type is mass prophylactic vaccination. The vaccine used in South America and in all British Colonies is made from chick embryos inoculated with an attenuated strain of yellow fever virus (known as 17D). Until recently the virus was always suspended in supposedly normal human serum. A clinical condition simulating infective hepatitis has occurred on a number of occasions several months after the inoculation of certain batches of vaccine. As the icterogenic agent which causes this condition was pre-

CUMULATIVE SUPPLEMENT 1945

sumed to have been in the apparently normal serum, the serum has been eliminated from the vaccine, which is now merely an embryo extract diluted with distilled water. The vaccine is prepared in the desiccated state in ampoules. Because of its instability, unless kept at low temperatures, it is distributed to special centres only and is not available at present for general distribution. The virus is living, but is so attenuated that reactions are negligible. For some reason as yet unexplained the inoculation may activate a latent malarial infection. It is considered that individuals are immune 10 days after vaccination. Fox and Cabral have recently found that with a satisfactory vaccine 98 per cent of persons inoculated still have immune bodies in their serum 4 years after inoculation. However, as batches of vaccine vary in their ability to immunize, and as there is considerable variation in the immune response of different individuals, it is considered advisable for reinoculation to be carried out every 2 years in the case of travellers entering regions in which vaccination is compulsory. It is required by law that any individual passing through an endemic yellow fever area and entering Egypt shall have been inoculated against yellow fever at least 10 days prior to entering the country.

General treatment*Chemotherapy*

None of the newly discovered drugs, such as sulphonamides or penicillin, has been found to be of any use in the treatment of the disease, the progress of which is too rapid for immune serum to be of any value. Symptomatic treatment and good nursing may help, but the final outcome depends entirely upon the patient's ability to combat the infection.

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Specific

In Narcotic Poisoning

The value of picrotoxin as an antidote to the barbiturates is described on page 280.

The investigations of Whitehead and Draper confirm the opinion that coramine is of only limited value. They found that it was antidotal against the lighter levels of avertin or ether narcosis, but ineffective against barbiturates. They found evidence that large doses might intensify respiratory depression, that the only local effect on the heart was harmful, and that, in experimental chloroform overdosage, the administration of this drug almost doubled the mortality.

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RETINA DISEASES

See also Surveys and Abstracts 1939, pp. 130 and 522; 1940, p. 510; 1941-2, p. 376.

DIAGNOSIS

Vital Staining of the Retina

Sorsby and his co-workers have, for a considerable time, been experimenting with vital staining of the retina with a view to its use in the diagnosis and assessment of disease of the fundus, especially of the retina.

1364

VASCULAR DISEASES

Venous Thrombosis

J. E. Jorpes has recently reported that, out of 20 cases of thrombosis of the central vein of the retina, about 10 recovered with normal or good vision after the administration of heparin.

1367

DETACHMENT

Treatment

Surgical

For the cure of detached retina, there is now more tendency to use indirect ophthalmoscopy with an extremely high candle-power illumination in tracking and localizing the retinal hole. Bipolar surface diathermy is being replaced in many centres by unipolar methods, the amperage being approximately doubled. Probably less stress is now laid on extensive drainage of the subretinal fluid and less reliance is placed on the value of the post-operation position in regard to the drainage of subretinal fluid.

1379

Jorpes, J. E. (1939) *Heparin: its Chemistry, Physiology and Application in Medicine*, London, p. 78.

Sorsby, A. (1940), Section 'Vital Staining of the Retina', *Modern Trends in Ophthalmology* (Sorsby, A., and Ridley, F.), London.

RHEUMATIC INFECTION, ACUTE

See Surveys and Abstracts 1939, pp. 135 and 523; 1940, p. 510; 1941-2, pp. 49 and 377.

1380

RHINOSCLEROMA

See Surveys and Abstracts 1940, p. 512.

1381

RHINOSPORIDIOSIS

See Surveys and Abstracts 1939, p. 524; 1940, p. 512.

1382

RICKETS

See Surveys and Abstracts 1939, pp. 38 and 524; 1940, p. 513.

1383, 1384

ROSACEA

Klaber and Wittkower, reviewing the pathogenesis of rosacea, state that a constitutional tendency to loss of contractile power of the smaller blood vessels of the face seems to be necessary for the establishment of the rosacea. Clinical examination of 50 cases showed no striking variation from previous serial observations. The history of spontaneous remissions was noted in several cases. The response to treatment of varied nature was erratic, both in degree and duration. Psychological investigation suggested that the type of personality and the effects upon it of emotional disturbances may be of fundamental importance in rosacea; 36 patients showed evidence of an abnormal degree of social anxiety which long antedated the onset of rosacea and 20 other patients had suffered from prolonged social or sexual stresses. The authors suggest that rosacea often results from emotional changes which may act directly by producing a 'permanent blush' or, perhaps more frequently, by lowering gastric tone may lead to a 'permanent flush'.

1386

Klaber, R., and Wittkower, E. (1939) *Brit. J. Derm.*, 51, 501.

SCARLET FEVER

See also Surveys and Abstracts 1939, pp. 77 and 525; 1940, p. 513; 1941-2, pp. 67 and 378.

AETIOLOGY

1387

The mode of spread of scarlet fever in a small closed community was investigated by R. Cruickshank and C. Muir; of 6 adult patients with influenza 4 developed clinical infection with fever (1 manifest scarlet fever) and from the nose of the fifth the same organism, Type I haemolytic streptococcus, was isolated. Members of the medical or nursing staffs did not harbour the organism. The organisms were found in the floor dust and atmosphere of the ward and were appreciably reduced in numbers by producing an antiseptic mist with resorcinol. (See also J. C. Thomas and M. van den Ende.)

BACTERIOLOGY AND MORBID ANATOMY

Blood Picture

The effect of sulphanilamide on the blood in scarlet fever was investigated by J. O. French who found little evidence of untoward effect on any of the elements except the polymorphonuclear leucocytes; at all periods, especially in the first week, there was a constant fall in the total white cell count, due to reduction of the neutrophils. The usual initial leucocytosis was absent in the untreated cases in 6.3 per cent, compared with 23 per cent in the sulphanilamide treated cases.

COMPLICATIONS, SEQUELAE, AND ASSOCIATED DISEASES

Gangrene

Only sixteen cases of gangrene complicating scarlet fever were reported by 1934 and in a dozen only were complete clinical data available. A female, aged 4, developed left suppurative otitis media on the thirty-fifth day of an attack of scarlet fever of moderate severity; 5 days later there was pain in the left foot which became blue and cold: endarteritis was diagnosed and heparin was given. On the forty-fifth day, left mastoiditis was present and the left leg swollen and of a purple hue as far as the malleolus; the arterial pulse could not be detected in the knee or thigh. A culture of *Staphylococcus aureus* was grown from the blood. Sulphonamides, blood transfusions, and vitamins were given and the mastoid signs abated. The foot became worse with sloughing of the skin of the outer aspect and exposure of peroneal muscles. On the fifty-sixth day of the disease amputation was performed below the knee well above the line of demarcation and a good recovery followed, although mastoidectomy was required a fortnight later (G. E. Breen).

TREATMENT

Prophylaxis

In a comprehensive review of the control of scarlet fever J. E. Gordon urged that notification should include doubtful or abortive cases in order to enable public health authorities to trace outbreaks. Period of isolation for those nursed in hospital or private houses should depend on age, severity, and presence or absence of complications. Need for hospital treatment should diminish as the size of families becomes less and housing improves. Current practice does not require freedom from haemolytic streptococci before release from isolation, but with improved therapeutics and individual isolation the majority would be free in 3 to 4 weeks.

G. F. Dick and Gladys H. Dick, the discoverers of the causal agent of scarlet fever, suggested as long ago as 1932 that oral administration of scarlet fever toxin in large doses should be employed for special cases, e.g. haemophiliacs and subjects abnormally sensitive to toxin and peptone used in its preparation. In 1940 they recorded their findings in 102 subjects immunized with dried toxin made up as 'enteric coated tablets'; at intervals from 2 to 8 weeks after taking up to 75 million 'skin test' doses 94.7 per cent were found to be Dick negative; they conclude that while successful for special cases this procedure is not for routine use.

Specific

Convalescent scarlet fever serum is claimed by W. Thalhimer to be an efficient therapeutic agent in doses of 20-100 cubic centimetres given intravenously. While the antitoxic content is admittedly lower than that of horse immune sera, human serum is regarded as containing more specific antibodies.

Sulphanilamide.—Sulphanilamide has been employed in scarlet fever on the grounds chiefly that the organisms responsible for the disease comprise certain strains of the haemolytic streptococci. Early reports, supported by meagre clinical observations, to the effect that sulphanilamide was effective in controlling the disease have been to a considerable extent discounted by later work. It now appears that sulphanilamide therapy does not influence the toxic stage of scarlet fever, that it has not reduced the incidence of complications, and that it is of no value in reducing the carrier state of discharged patients. Its value as a prophylactic in non-immune contacts is still unsettled. Unless further evidence becomes available

deficiency; (6) in all cases of serious injury. Patients for operation should be saturated beforehand.

Anson, G., and Walter, R. (1748) *A Voyage round the World in the Years 1740-44*, London, p. 241.

Hunt, A. H. (1941) *Brit. J. Surg.*, 28, 436.

SENESCENCE AND SENILITY

1394 See Surveys and Abstracts 1939, p. 528; 1940, p. 518; 1941-2, p. 379.

SEPTICAEMIA AND BACTERIAEMIA

See also Surveys and Abstracts 1939, p. 530; 1940, p. 519; 1941-2, pp. 4 and 58.

METHODS OF BLOOD CULTURE

1395 Hoare's recent experiments indicate that the routine use of 'liquoid' as an anti-bactericidal substance in blood-culture media should not be recommended, as it was found to be definitely unfavourable to the growth of anaerobic streptococci, which are commonly present in the blood in puerperal fever and less commonly in other conditions. Sterile trypsin had no such inhibitory effect.

Various methods of blood culture and the selection of suitable media have been investigated by Penfold *et al.* with a view to determine the relative value of the various media and to establish the most satisfactory series for routine investigation. They used two methods: routine blood cultures on patients, and blood cultures inoculated artificially with organisms recently isolated from human patients. Of 160 routine blood cultures 33 gave positive results. The organisms most commonly isolated were *Staph. pyogenes* and *Strep. viridans*. Others included the non-haemolytic streptococcus, *Pneumococcus*, *Haemophilus para-influenzae*, *Bact. coli* (one atypical), *Strep. haemolyticus*, and *Bact. typhosum*.

In collecting the specimens of blood it is most important to observe strict asepsis otherwise contamination is very probable.

The results of this investigation indicate that for general routine work the following media should be used: solid media—saponin broth with agar, and glucose trypsin broth with agar; Hartley's broth and, when micro-aerophilic or anaerobic organisms are suspected, Robertson's meat medium. The saponin medium compares favourably with all the other media particularly in the isolation of *Strep. viridans*; when this organism was isolated the saponin medium gave positive results in every case and as a rule sooner than the other media. The glucose trypsin broth gave a lower percentage of positive results than any of the other media; the reason for recommending it is that on several occasions it gave an early growth of *Staph. pyogenes*, preceding those with other media by 12 to 48 hours.

Experiments with liquoid have been disappointing and in no type of infection was it superior to other media. There was therefore no indication for its continued use in routine work.

SIGNIFICANCE OF POSITIVE BLOOD CULTURES

Following the inquiry into bacteriaemia following dental extractions, Elliott (1939, a) has investigated bacteriaemia following within a few minutes of tonsillectomy. In 100 cases 38 per cent of the patients showed a transient bacteriaemia after tonsillectomy, irrespective of the operative technique employed—guillotine or blunt dissection. The organisms isolated included *Strep. pyogenes*, *Strep. viridans*, *Pneumococcus*, *Haemophilus influenzae*, *Staphylococcus*, and *Corynebacterium*. In most of the patients operated upon in the morning, the temperature rose to 99 or 100° F. by the evening, but this pyrexia was not related to the existence of a demonstrable bacteriaemia or to the presence of any particular organism. It was possible to match serologically the strain of *Strep. pyogenes* recovered from the blood with the strain isolated from the corresponding tonsils after removal.

Examination of the tonsils of 137 patients undergoing tonsillectomy showed the presence in them of haemolytic streptococci in 87 (64 per cent); 44 of these cultures were examined serologically and 39 of them were found to belong to group A, one to group B, and one to group C (Lancefield). From these observations it is obvious that transient bacteriaemia is not uncommon after tonsillectomy and that the diversity of bacteria which may circulate in the blood is greater than after dental extraction, when the organisms are almost exclusively non-haemolytic streptococci. From time to time tonsillectomy is followed by subacute bacterial endocarditis, and recrudescence of acute rheumatism and acute nephritis. These observations indicate the possible explanation of such cases, and in this connexion it is of interest that occasionally in subacute infective endocarditis the causal organism may belong to the haemophilus group, which was one of the groups isolated in this experiment. It is also noteworthy that pathogenic organisms such as *Strep. pyogenes* may circulate in the blood for short periods and in small numbers without producing any obvious ill effects. The fact that about 60 per cent of patients admitted to hospital for tonsillectomy carry *Strep. pyogenes* in the throat emphasizes the risk of cross infection in otorhinological wards.

Elliott (1939, b) has again reported on the transient streptococcal bacteraemias which frequently follow extraction of teeth, particularly in cases in which there is severe chronic infection of the gums. In such cases bacteria may gain entrance into the blood stream irrespective of operative procedures, and probably as a result of minor degrees of gum injury such as is produced by biting on a loose tooth. Acute apical infections do not appear to be particularly associated with blood infection of this kind, the focus of infection apparently being effectively walled off by the associated inflammatory reaction. In the production of these post-operative bacteraemias, infection appears to be more important than trauma, since, when infection is marked, very slight degrees of gum injury are sufficient to produce blood stream invasion. Streptococcal bacteraemias were found to occur in 86 per cent of cases of severe gum infection following the mere 'rocking' of teeth, or even of one tooth only. In the complete absence, however, of the type of trauma produced by rocking of a tooth during its extraction, removal may be carried out without producing a heavy bacterial shower in the blood. As a rule these transient bacteraemias produce no permanent ill-effect, but there is some evidence that, in subjects with abnormal heart valves, they may lead to subacute bacterial endocarditis. Prevention of such bacteraemias may be achieved by reduction or elimination of gum infection and by manipulating an infected tooth as little as possible during extraction.

STREPTOCOCCAL BACTERIAEMIA AND SEPTICAEMIA

Loewenthal experimented with mice infected with *Streptococcus pyogenes* Group A, in the hope of reducing the dose of sulphanilamide necessary to protect them by administering simultaneously antistreptococcal serum. This line of attack was suggested by the fact that, as drugs of this group are not bactericidal but only bacteriostatic, the co-operation of phagocytes is required in order to rid the blood of the bacteria. Mouse-protection tests and therapeutic trials both indicated that these two therapeutic agents acted in a different but complementary manner, and that the protective effect of either serum or sulphanilamide was enhanced if used in conjunction with the other agent.

Elliott, S. D. (1939, a) *Lancet*, 2, 589.

— (1939, b) *Proc. R. Soc. Med.*, 32, 747.

Hoare, E. D. (1939) *J. Path. Bact.*, 48, 573.

Loewenthal, H. (1939) *Lancet*, 1, 197.

Penfold, J. B., Goldman, J., and Fairbrother, R. W. (1940) *Lancet*, 1, 65.

SEX HORMONES

See also Surveys and Abstracts 1939, pp. 17, 34, 108, and 531; 1940, pp. 20, 21, 55, 131, and 520; 1941-2, pp. 4, 20, 81 and 381.

USE OF SEX HORMONES IN TREATMENT OF MENSTRUAL AND CLIMACTERIC DISORDERS

Preparations and Standardization of Female Sex Hormones and Gonadotrophic Hormones

The Third International Conference on the Standardization of Hormones was held at Geneva in August 1938. It was agreed that it was both desirable and practicable to establish international standards for the gonadotrophic substance of urine of pregnancy; the thyrotrophic substance of the anterior lobe of the pituitary gland; the lactogenic (crop-gland-stimulating) substance of the anterior lobe of the pituitary gland ('prolactin', 'galactin', 'mammatrophin'); and the gonadotrophic substance of the serum of the pregnant mare. Arrangements were made for the preparation of standards of these substances and for the definition of the units in each case. No decision was reached as to the choice between the suffixes 'tropic' and 'trophic' in the descriptive terms describing the hormones, but in their report the Committee adopt the use of 'trophic'.

1397

CLINICAL USE OF MALE SEX HORMONE

Preparations of Male Sex Hormone

The administration of testosterone by mouth was mentioned in Vol. XI, p. 108; recently a derivative—methyl testosterone—has been found to have greater effect by this route. It is suggested that the methyl group protects the active hydroxyl group from the destructive effects of the fermentative processes in the alimentary canal. Foss has shown that this new product is about twice as potent when tried on an eunuch, whereas in cases of hypogonadism it is effective and rapid in action, and in every way preferable to injection. At present, only the price of this preparation can prohibit its generalized replacement of injection of testosterone propionate when androgen therapy is indicated.

1398

Therapeutic Use

Hypogonadism is one of the most important indications for androgen therapy. Cases of adiposo-genital dystrophy and simple hypogonadism are best treated at

the time of puberty and show rapid development of the penis and secondary sexual characters. It is wise to combine thyroid therapy and so adjust the whole normal bodily form.

Oral therapy with methyl testosterone is adequate for cases at puberty and small doses only are required—such as 2.5 mg., 4 times daily, for about 6 months. The oral route may prove to be adequate also for older patients, but sometimes injections of testosterone propionate, 50 to 100 mg. daily, may be necessary for adults with genital hypoplasia.

Testicular development is achieved by combined treatment with prolan or pregnyl or other makes of chorionic gonadotrophin.

Testosterone propionate can be used for treating climacteric conditions, but the dose required is high, 30 to 50 mg. per week (Kurzrok, Birnberg and Livingston), and relapses occur on withdrawal. Probably it is best indicated for the poly-oestrin phase, but oestrogens must be preferable and are effective in smaller dosage for the anoestrin phase, and for flushes of the climacteric.

III Effects

Doses of 3,000 to 5,000 mg. of testosterone propionate given over a period of months will cause undesirable side-effects in most women, namely an acneiform eruption on the face and body, growth of hair on face and body, deepening of the voice, and enlargement of the clitoris. Of these effects all except the enlargement of the clitoris may be temporary, although it may take some months after treatment has ceased for the voice to return to normal, or for excess hair to disappear. Androgen therapy for women should therefore be used with extreme caution as the effective dose is very near the toxic dose and such treatment is best given by those experienced in its use.

Foss, G. L. (1939) *Brit. med. J.*, 2, 11.

Kurzrok, L., Birnberg, C. H., and Livingston, S. (1939) *Endocrinology*, 24, 347.

Report of the Third International Conference on the Standardization of Hormones held at Geneva in August, 1938. *Quart. Bull. Hlth Org. L.o.N.* (1938), 7, 889, abstracted in *Endocrinology* (1939), 25, 318.

SEXUAL BEHAVIOUR AND ABNORMALITIES

1399

See Surveys and Abstracts 1940, pp. 60 and 520; 1941-2, p. 385.

SHOCK AND COLLAPSE

See also Surveys and Abstracts 1939, p. 537; 1940, pp. 11 and 527; 1941-2, pp. 1, 8, 38 and 385.

AETIOLOGY

1400

There have been no convincing new investigations on the aetiology of shock. The question of the influence of nerve-impulses in causing shock has been the subject of investigations with opposing conclusions. Slome and O'Shaughnessy concluded that nerve-impulses play an important part, whereas Blalock and Cressman, as the result of rather similar experiments, conclude that they are not of leading significance, the chief factor in the production of shock after trauma being fluid-loss in the traumatized area.

Loss of Body Fluid

Haemo-concentration accompanying shock is described by V. H. Moon as the outward drainage of plasma due to increased permeability of capillary endothelium, resulting in an increase in erythrocytic concentration, circulatory deficiency, capillary dilatation, oedema, blood stasis, and fall of blood pressure. Many substances and agents can induce haemo-concentration, including aqueous extracts of normal tissue, peptone, foreign protein, bile, emetine, histamine, poisons and venoms, products of tissue autolysis, intestinal manipulation, circulatory obstruction, anaphylactic shock, allergic pollen reaction, intestinal obstruction, serious infection, burns, trauma, and surgical shock. Intravenous injections of substances which cause external wheals, give the syndrome of shock. Haemo-concentration has been observed in cases of haemorrhage (haemo-dilution) due to war wounds. This provides a distinction between simple haemorrhage and shock. The author attributes haemo-concentration to the production of an unknown substance, not necessarily toxic, from damaged tissues, affecting the general permeability of capillary endothelium. The induction of shock by products of tissue autolysis and the presence of high non-protein nitrogen content of the blood during shock suggest proteolytic products as a possible agent. Experiments done by others to prove that shock following haemorrhage is due to localized fluid-loss are unreliable, as falling blood pressure was the sole criterion of shock and anaesthetics alone may effect this. The author, moreover, induced shock in dogs by peritoneal injections of freshly ground muscle, without pain and haemorrhage; only a slight local anaesthetic was used. Shock was produced and a necropsy showed stasis and oedema in remote

organs, a post-mortem feature of shock due to burns. This indicates a wide-spread and not a localized agent. The efficacy of tannic acid is attributed to tissue coagulation preventing the spread of the agent. Intravenous injections of dyes during experimental shock also show plasma outflow far from the seat of injury. Experimental evidence dismisses sympathetico-adrenal hyperactivity as a cause of haemo-concentration. Failure of the adrenal cortex leads to loss of capillary tonus, recoverable by the administration of the hormone. Haemo-concentration is noted in the critical stages of Addison's disease. A compensating mechanism is observed by sympathetic vasoconstriction, splenic discharge, myocardial stimulation, resulting in a momentary recovery of blood pressure leaving the rate of flow still deficient. Breakdown of this mechanism is followed by a rapid fall in blood pressure. Haemo-concentration thus gives warning of impending circulatory collapse when blood pressure is still high. The importance of haemo-concentration in infection was demonstrated by post-mortem examinations of influenza patients with full symptoms, no haemo-concentration being revealed in the non-fatal cases; a useful point for prognosis. Cats dying from experimental diphtheritic infection have been kept alive by the perfusion of the heart with defibrinated blood. Thus circulatory collapse is not due to myocardial deficiency, but to fall in blood volume. Attention is drawn to the self-perpetuating cycle of capillary atony producing anoxia and vice versa, leading to death. The author emphasizes the practical significance of haemo-concentration and suggests that more attention should be given to the phenomenon.

HYPOTHESES OF SHOCK

Toxaemia

Allen supports the 'toxaemic' theory. He produced shock in rats by ligature of limbs; when the ligatures were removed after 3 or more hours, or less if more than one limb had been ligatured, marked shock developed, with increased concentration of the circulating blood, reduction of its volume, and migration of fluid to the tissues. Amputation of the asphyxiated limb before release of the ligature, or shortly afterwards, prevented the onset of shock, an observation explicable on the 'toxaemic' hypothesis: moreover, refrigeration of the asphyxiated limbs during the asphyxia inhibited the subsequent shock, whereas warming augmented it. These observations suggested that the toxic substance was a product of the disordered metabolism during the asphyxial period.

TREATMENT

Therapeutically, Allen found that, after shock was fully developed, the only effective measure was blood transfusion, but the effect of this was transient, and it did not seem to prevent an ultimate fatal outcome. If started before shock was present, saline infusions were the most effective therapeutic measure, blood being less effective at this stage, separated plasma less effective still, and separated corpuscles and acacia solutions completely ineffective. These observations seem to be in harmony with clinical experiences in the human subject.

On the ground that the clinical and biochemical changes in shock resemble those of adrenal cortical insufficiency, as exemplified in Addison's disease, it has been suggested that cortical extract might be useful in the treatment of shock. This has been tried with promising but as yet inconclusive results in the 'toxaemic' shock following burns (Wilson *et al.*).

Cortin.—H. Selye, C. Dosne, L. Bassett, and J. Whittaker of Montreal follow up the work of Selye (1936) on the syndrome of 'the alarm reaction' by a report on the experimental therapeutic value of the adrenal cortex in traumatic shock and allied conditions. The alarm reaction 'represents the somatic expression of the call to arms of the body's defence mechanism', and is characterized by many degenerative lesions and biochemical changes occurring in shock, for which the following concise definition is suggested: 'a condition of suddenly developing general damage'. The symptom-complex of the alarm reaction is divided into two phases, the first of shock and the second of counter-shock. The period of shock lasts, according to the severity of the injury and the animal's resistance, from 1 to 36 hours, in which many animals die. It is immediately followed by an entirely different set of symptoms which are the reverse of those in shock. This second phase is that of counter-shock. As adrenalectomized animals do not pass into the second phase, and as in other animals the adrenals are much enlarged, the cells of the cortex showing activity as do also the chromaffin cells of the medulla, it appears that the adrenals, and especially the cortex, play an important part in counter-shock. Further, the greater the enlargement of the adrenals the more extreme is atrophy of the thymus; these two structural changes are phenomena of counter-shock, whereas the first stage, that of shock, may be correlated with relative insufficiency of the adrenal cortex. Experiments on rats dealt with the therapeutic effects of adrenal cortical preparations on shock; cortin (corticosterone) was extremely active in combating traumatic shock, whereas desoxycorticosterone acetate was not. Repeated small doses of cortin were more effective than a large single dose of the same total amount. P. G. Weil, B. Rose,

and J. S. L. Browne, also of Montreal, report the results of the treatment of experimental traumatic shock in rabbits by two methods: (1) administration of both cortin (corticosterone) and desoxycorticosterone acetate; the mortality rate was 19 per cent; (2) desoxycorticosterone acetate; the mortality rate was 46 per cent. The mortality rate among 58 rabbits in which traumatic shock was induced, but adrenal cortex preparations were not given, was 62 per cent. It is suggested that the administration of adrenal cortical substances before and after operations and in other causes of shock, such as injuries, infections, and burns, may be clinically important.

- Allen, F. M. (1939) *Arch. Surg., Chicago*, **38**, 155.
Blalock, A., and Cressman, R. D. (1939) *Surg. Gynec. Obstet.*, **68**, 278.
Moon, V. H. (1941) *Amer. J. clin. Path.*, **11**, 361.
O'Shaughnessy, L., and Slome, D. (1935) *Brit. J. Surg.*, **22**, 589.
Selye, H., Dosne, C., Bassett, L., and Whittaker, J. (1940) *Canad. med. Ass. J.*, **43**, 1.
Slome, D., and O'Shaughnessy, L. (1938) *Brit. J. Surg.*, **22**, 900.
Weil, P. G., Rose, B., and Browne, J. S. L. (1940) *Canad. med. Ass. J.*, **43**, 8.
Wilson, W. C., Macgregor, A. R., and Stewart, C. P. (1938) *Brit. J. Surg.*, **25**, 826.
— Rowley, G. D., and Gray, N. A. (1936) *Lancet*, **1**, 1400.

SILICOSIS

- 1401 See Surveys and Abstracts 1939, p. 537; 1940, p. 529; 1941-2, p. 389.

SIMMONDS'S SYNDROME

- 1402 See Surveys and Abstracts 1939, p. 538, and 1940, p. 530; 1941-2, pp. 92 and 390.

SKIN DISEASES: I.—AFFECTIONS DUE TO INSECTS AND ACARINES

- 1403-1404 See Surveys and Abstracts 1940, p. 531; 1941-2, p. 390.

SKIN DISEASES: II.—OCCUPATIONAL DISEASES

See also Surveys and Abstracts 1941-2, p. 392.

DEFINITION

- 1405 Table II, Vol. XI, p. 163. The figures for 1937 and 1938 are as follows:

	A	B	A	B	A	B	A	B
1937	784	2650	3	19	74	60	1	25
1938	782	2735	1	21	79	65	3	16

CHROME ULCERATION

Incidence

Corrigendum

- 1407 In Vol. XI, p. 174, substitute Table VI by that given below.

TABLE VI.—Occurrence of Chrome Ulceration in Great Britain During the Period 1920 to 1940

	1920-26	1927-33	1934-40	TOTAL
Dyeing and finishing —	201	111	35	347
Manufacture of bichromates —	125	40	40	205
Chrome tanning —	26	38	37	101
Colours and dyes —	13	14	16	43
French-polishing —	21	9	..	30
Printing and engraving —	8	8	3	19
Paper and card manufacture —	7	4	1	12
Chromium plating —	..	291	456	747
Anodic oxidation —	..	28	78	106
Chromating of metals —	36	36
Miscellaneous —	8	11	32	51
Total	409	554	734	1,697

SKIN DISEASES: III.—LOCALLY INOCULATED INFECTIONS

See also Surveys and Abstracts 1940, p. 532; 1941-2, p. 392.

Corrigendum

- 1409 Vol. XI, p. 183, 11th line of paragraph 1, substitute '*Erysipelothrix muriseptica*' for '*Erysipelothrix (B. suispestifer)*'.

Streptococcus

Chronic Streptococcal Ulceration

- 1410 Chronic streptococcal ulceration with the formation of daughter abscesses burrowing into the subcutaneous tissue have been further investigated by Meleney,

who claimed that the causal organism was a micro-anaerobic haemophilic streptococcus. If this organism is grown anaerobically, after 2 days it will grow aerobically. It then shows the 'alpha' type of haemolysis. Meleney treated the ulceration by laying open all the pockets in the wound and then carefully packing with zinc peroxide cream (zinc peroxide gives off oxygen slowly for 24 hours). According to F. L. Meleney and H. D. Harvey sulphanilamide given alone produces no favourable effect, but they noted acceleration of healing when it was used simultaneously with zinc peroxide in the wound.

Treatment of Recurrences of Ulceration

According to Clarkson (personal communication) extensions of ulceration, with tenderness just beyond the edge of the wound, redness, and swelling, associated with a slight rise of temperature, have responded to treatment with sulphanilamide, 4 grams a day for 2 days. The subcutaneous tissue inflammation was re-absorbed without the formation of an abscess breaking down and becoming confluent with the ulcerated area.

SKIN DISEASES: IV.—TUBERCULOSIS

See Surveys and Abstracts 1939, p. 538.

1411

SKIN DISEASES: V.—TUMOURS

See also Surveys and Abstracts 1939, p. 539; 1940, p. 533; 1941-2, p. 393.

INNOCENT TUMOURS

Derived from Sweat-Glands

Fox-Fordyce Disease

Szép has noticed the occurrence of symptoms due to endocrine imbalance in patients with Fox-Fordyce disease and ascribed this condition to dysfunction of one of the glands, probably the ovaries. He treated a patient with follicular hormone and X-ray irradiation, and in 3 months from the beginning of treatment the condition was greatly improved.

1412

Derived from Bones, and Calcinosis

Calcinosis

Atkinson and Parkes Weber reviewed the subject of cutaneous and subcutaneous calcinosis, grouping cases in which the deposits are confined to special areas as calcinosis circumscripta, and the more serious and often fatal type in which the distribution of the lesions is very variable as calcinosis universalis. They did not include cases of calcinosis in which the skin and subcutaneous tissues are not involved. They recorded the results of blood examination in 20 cases of calcinosis circumscripta and 36 of calcinosis universalis. These did not show any particular abnormality in the haemoglobin or red cells; the leucocytes ranged from 14,500 to 3,500, with polymorphonuclears 76 to 19 per cent (circumscripta), and 23,600 to 4,250, with polymorphonuclears 90 to 44 per cent (universalis); eosinophilia was sometimes present in both forms. The constituents of the blood and metabolic studies were reported in detail; the deposits chiefly contained calcium phosphate and calcium carbonate. The highest blood calcium recorded was 28 mg. per 100 c.cm. (circumscripta). The association of scleroderma with calcinosis circumscripta (40 per cent of 137 cases), and to a less extent with calcinosis universalis (32 per cent of 78 cases) was noted. Raynaud's disease and other vasomotor disturbances were also often associated.

MALIGNANT TUMOURS

Derived from Superficial Layers of Epithelium

Intra-Epidermal Carcinoma

Paget's disease of the skin.—Weiner has discussed the histogenesis of Paget's 'eczema' and the 57 reported extramammary cases. He concluded that the disease is due to intra-epidermal metastases from a carcinoma of the apocrine sweat glands.

1413

Stout has reported a case of intra-epidermal melanoma (naevocarcinoma) without pigment and closely resembling Paget's disease, and has discussed 6 similar cases previously reported. The site of the tumour is of diagnostic importance, for in the mammary, axillary, or genital zones, where Paget's disease may occur, it may be very difficult to distinguish the 2 conditions, whereas in other sites a diagnosis of melanoma is more probable.

Melanotic Carcinoma

Corsi reported the clinical course of three cases of *mélânose circonscrite pré-cancéreuse* and the results of histological examinations made by Klaber, 2 in women, aged 76 and 87, and one in a man aged 47. The cases were watched through 2, 5, and 12 years. Nodules appeared from time to time and in 2 of the cases were treated by radon seeds. Histologically they differed widely and were difficult to interpret. In the melanotic areas without tumour formation in one case Pagetoid cells were present. The clinical course was more benign than the histology suggested.

SYSTEMIC CONDITIONS

Malignant

Hodgkin's Disease

1415

A case of ulcerative Hodgkin's disease of the skin in a girl, aged 15, was reported by Pessin and Pohle, the twenty-ninth reported case since 1906. It was thought that an osteomyelitic process in the sternum preceded the skin lesions. An abscess developing in the manubrium was curetted twice; 6 months after the first curettage a granulomatous mass had developed at the site of the wound, and the adjacent skin contained elevated white, pinkish, and livid red nodules, and a small lymph node was palpable in the left supraclavicular region and another in the left axilla. Five months later there was a large ulcer over the sternum, and biopsy of a lymph gland revealed typical Hodgkin's disease. Under X-ray therapy the ulcer healed; the patient survived for at least a year (until November 1937) but died after some months (interval not stated).

Atkinson, F. R. B., and Weber, F. P. (1938) *Brit. J. Derm.*, **50**, 267.

Corsi, H. (1939) *Brit. J. Derm.*, **51**, 86.

Dowling, G. B. (1939) *Brit. J. Derm.*, **51**, 82.

Meleney, F. L., and Harvey, H. D. (1939) *Ann. Surg.*, **110**, 1067.

Pessin, S. B., and Pohle, E. A. (1938) *Amer. J. Cancer*, **34**, 220.

Stout, A. P. (1938) *Amer. J. Cancer*, **33**, 196.

Szép, E. (1938) *Arch. Derm. Syph., Wien*, **77**, 124.

Weiner, H. A. (1937) *Amer. J. Cancer*, **31**, 373.

SMALLPOX

INCIDENCE AND EPIDEMIOLOGY

1416

According to official figures there were fewer cases of smallpox in the United States of America in 1940 than in any previous year. The 2,839 cases reported represented a drop of 709 from the previous year. In Canada in 1940 there were only 11 cases reported and no deaths.

TREATMENT

Prophylactic

Vaccination

Rivers, Ward, and Baird described the immunity resulting from the primary intracutaneous vaccination of 331 children with a strain of vaccinia virus cultivated under aseptic conditions in association with chick embryo tissue. Of this group 82, or 25 per cent, were immune and 249, or 75 per cent, responded with accelerated reactions. These authors attributed the failure to develop a solid immunity following intracutaneous vaccination to the attenuation of their strain of virus as a result of repeated subculture. They suggested that individuals vaccinated in this way should be revaccinated dermally 6 months to 1 year later with a potent vaccine lymph. In their view, the discomfort and disability resulting from primary vaccination with vaccine lymph would be avoided by this procedure and a lasting immunity to smallpox would result.

Henderson and McClean described the result of intracutaneous and subcutaneous vaccination with a bacteria-free elementary body suspension of vaccine virus prepared directly from vaccine pulp; 131 adults and 197 children were inoculated. It appeared that there was a definite correlation between the appearance of a typical epidermal vesicle following the primary vaccination and the subsequent development of immunity. Of 75 individuals who developed vesicles, 72 were completely refractory to revaccination; 2 of the remaining 3 developed modified lesions on revaccination without vesicle formation. Of 89 subjects who did not develop vesicles, 58 produced typical vaccinal reactions on revaccination. These authors suggested that this result might be due to the epidermotropic character of the strains of vaccine virus in common use for the preparation of vaccine lymph and that further investigation with other strains less exclusively epidermotropic might show that a satisfactory immunity can be developed without vesicle formation.

Symptomatic

McCammon reported the results of treatment of 7 cases of smallpox: 3 were treated symptomatically and all had typical rashes; 4 were given sulphanilamide in doses of 5 to 10 gr. every 3 hours; 3 of these had only an evanescent macular eruption and one had only 3 pustules. A similar abortive attack following the use of prontosil rubrum was reported by King and De Rozario.

Henderson, R. G., and McClean, D. (1939) *J. Hyg., Camb.*, **39**, 680.

King, C., and De Rozario, K. A. (1938) *J. R. Army med. Cps*, **71**, 404.

McCammon, W. O. (1939) *J. Amer. med. Ass.*, **112**, 1936.

Rivers, T. M., Ward, S. M., and Baird, R. D. (1939) *J. exp. Med.*, **69**, 857.

Statist. Bull., Metrop. Life Insur. Co. N.Y. (1941) **22**, 6.

SPEECH DEFECTS

See Surveys and Abstracts 1939, p. 542; 1940, p. 535.

1417-1424

SPINAL CORD DISEASES

See Surveys and Abstracts 1939, pp. 120 and 543; 1940, p. 536; 1941-2, p. 395.

1425-1433

SPINE, DISEASE AND DEFORMITIES

See Surveys and Abstracts 1939, p. 544; 1940, p. 536; 1941-2, pp. 14 and 396.

1434-1445

SPLEEN DISEASES

See also Surveys and Abstracts 1939, p. 546; 1940, p. 541; 1941-2, p. 397.

RETICULO-ENDOTHELIOSIS OF THE SPLEEN**Reticulo-Endothelial System in Splenic Disease***Reticuloses and Reticulo-Sarcoma*

Classification.—A few years ago it was appreciated that there existed a group of disease pictures akin to Hodgkin's disease which were usually labelled by such names as 'atypical Hodgkin's', 'malignant Hodgkin's'. An attempt was made to develop a reasonable classification of this group of diseases affecting the reticular cells of the spleen and lymphatic glands along the following lines (A. H. T. Robb-Smith).

1451

1. *Reticulosis* is defined as a progressive hyperplasia of reticular tissue with differentiation to one or more cell types. Important subdivisions of this group include: (a) lymphoid, myeloid, and monocytic leucoses (leukaemias); (b) storage reticuloses-lipoidoses, Gaucher's disease; (c) fibromyeloid reticulosis—Hodgkin's disease; (d) reticulum-celled and histiocytic reticuloses.

2. *Reticulo-sarcomas*. This group includes: (a) undifferentiated reticulum-celled sarcomas; (b) lymphosarcoma; (c) 'plasmacytome' (multiple myelomatosis—lymph gland and spleen involvement rare); (d) mixed type (polymorphic reticulo-sarcoma = 'malignant Hodgkin's'). This classification serves a useful purpose in the study of a number of obscure diseases of the reticulo-endothelial system. The clinical and pathological pictures of the reticuloses grouped under (a), (b), and (c) above are well recognized. Under group (d) R. B. Scott and A. H. T. Robb-Smith have recently described a series of cases characterized by fever and wasting, lymphatic gland enlargement, enlargement of spleen and liver, jaundice, purpura and anaemia with leucopenia. The cases ran a fatal course and at post mortem there was found a systematized hyperplasia of histiocytes in the affected reticulo-endothelial tissues. Some of these contained red cells or red-cell debris.

Skin manifestations.—In reporting a case of mycosis fungoides L. Berman notes that apart from the skin lesions which finally fungate, liver, spleen, and lymphatic glands are frequently involved. Mutations into various histological forms are reported, e.g. to typical Hodgkin's disease (H. MacCormac). Monocytic leukaemia may begin by involving the skin and resemble mycosis fungoides. The histological lesion of mycosis fungoides is thus non-specific. Three distinct histological types are recognized: (1) Hodgkin's type; (2) reticulum-celled sarcoma; (3) lymphosarcoma. Mycosis fungoides may thus be regarded as a disease of the reticular cells which may be either a reticulosis or a reticulo-sarcoma.

Berman, L. (1940) *Arch. Path.*, **29**, 530.

MacCormac, H. (1941) *Brit. med. J.*, **2**, 645.

Robb-Smith, A. H. T. (1938) *J. Path. Bact.*, **47**, 457.

Scott, R. B., and Robb-Smith, A. H. T. (1939) *Lancet*, **2**, 194.

SPRUE, TROPICAL

See Surveys and Abstracts 1940, p. 542; 1941-2, pp. 26 and 398.

1453

STERILITY

See also Surveys and Abstracts 1939, pp. 30, 157, and 548; 1940, p. 543; 1941-2, pp. 21 and 399.

STERILITY IN THE MALE**Diagnostic Testicular Biopsy**

In the more obscure cases of male sterility or sub-fertility, when other methods have failed to provide a diagnosis, great help can be obtained from carrying out a testicular biopsy. This can generally be done under local anaesthesia, and without risk to the testicle. All that is necessary is to puncture the tunica albuginea after exposure of the testicle. The small button of testicular tissue that extrudes is cut off with a pair of iridectomy scissors and examined microscopically. This method provides accurate information about the state of the tubules, and is invaluable.

1457

STERILIZATION

See also Surveys and Abstracts 1939, pp. 158 and 549; 1940, p. 23; 1941-2, p. 22.

STERILIZATION OF THE MALE

Incision.—Vol. XI, p. 474, paragraph 3: for the third and fourth sentences (lines 4 to 8) substitute the following:

1460

This structure is then carefully separated by dissection from the other constituents of the cord, and two clamps are applied to it at least one inch apart. The intervening portion of the vas is then excised, and the divided ends held by the clamps are ligatured with silk.

STOMACH, TUMOURS AND SOME OTHER CONDITIONS

1461-1464 See Surveys and Abstracts 1939, p. 549; 1940, p. 544; 1941-2, pp. 13 and 400.

STRABISMUS

See also Surveys and Abstracts 1939, pp. 131 and 551; 1940, p. 546; 1941-2, p. 402.

COMITANT (CONCOMITANT) OR NON-PARALYTIC SQUINT

Aetiology

1465

In 1939 F. B. Chavasse published fresh material which proved that a fair number of cases of apparently comitant squint in reality start as a paralytic lesion. For example, the external rectus action can be interfered with in a number of ways during the process of birth. Thus the nerve supply may become impaired by involvement of the nucleus of the sixth nerve in one of the many minute interpositive haemorrhages which may occur, or by involvement of the nerve trunk in larger haemorrhages, or in basal fractures; further, the muscle may be put out of action by rupture of its sheath or by haemorrhages into its substance. That something of this kind is not uncommon is demonstrated by the finding of adhesions between the external rectus and the sclera at some operations for the cure of convergent squint. Although recovery seems to occur from the early lesion, the deviation becomes perpetuated in a more or less comitant convergence, which persists after the initial palsy can no longer be demonstrated. The position becomes more complicated when a muscle such as the superior oblique is involved (e.g. by injury to its pulley) and compensatory spasm is evoked in its antagonizing elevator, viz. the inferior oblique of the other eye. Cases of so-called spasm of the inferior oblique are not very rare and are a fruitful source of ocular torticollis. The effect of the lesion becomes evident on adduction of the eye when it is seen to shoot upwards on nearing the end of its movement towards the nose. Other causes suggested for spasm of the inferior oblique include over-development of the muscle or an abnormality of its insertion. Whatever the cause of the lesion its effect can be dealt with satisfactorily by myectomy of the muscle through a conjunctival incision.

Chavasse, F. B. (1939) *Worth's Squint or the Binocular Reflexes and the Treatment of Strabismus*, 7th ed., London.

SYMPATHETIC AND PARASYMPATHETIC NERVOUS SYSTEM

1466

See Surveys and Abstracts 1939, pp. 121 and 552; 1940, p. 546.

SYPHILIS

See also Surveys and Abstracts 1939, pp. 151 and 553; 1940, pp. 87 and 547; 1941-2, pp. 102 and 403.

BACTERIOLOGY

Staining Methods

1467

Manouélian, by the use of Séguin's modification of the Fontana-Tribondeau method of staining *S. pallida*, has established that this organism divides like any other spirochaete, namely transversely, and often so that it is broken up into fragments as small as half a spiral, which he calls spirochaetogenic granules. They are distinguished from debris or artifact by their adherent tags of periplasm which retain to some extent the spiral shape of the parent organism. Such granules are found chiefly in resolving and old lesions and in lymphatic glands of patients under treatment. In such cases few or no typical *S. pallida* are found, and this fact has led Levaditi to advance the theory that the organism of syphilis has a life history in which it assumes forms quite different from the original spirochaete. Manouélian, however, disclaims any relation between his spirochaetogenic granules and the granules and other forms described by Levaditi.

Simon and Mollinedo have recommended that Séguin's method of staining be applied to gland juice in suspected cases. In the gland juice of 15 cases they found typical spirochaetes 7 times by the dark-ground method and 12 times by the Séguin method, but spirochaetogenic granules in 14.

Knisely has rediscovered the collargol modification of the Burri method of demonstrating *S. pallida* in films. In the Burri technique some of the discharge is mixed with Indian ink and spread on a microscope slide like a blood film. The spirochaete stands out as a white unstained spiral against a black or dark-brown background. The difficulty in it is to obtain a perfectly smooth emulsion of Indian ink. In Benians's modification, instead of Indian ink, a 2 per cent solution of Congo red is used, and after the film has been spread it is treated with 1 per cent hydrochloric acid in absolute alcohol; the background is blue. In Harrison's modification, as in Knisely's recently published, a 1 in 20 solution of collargol is used and the

background is light brown. In both of these modifications the background is quite smooth.

An additional technique for the identification of *S. pallida* in fresh serous smears was described by Krajian. The lesion is rubbed with a swab dipped in alcohol until its surface bleeds. When all bleeding stops, a clear serous exudate appears which is smeared on a slide and dried in air. Each smear is flooded for 5 minutes with a warm solution consisting of uranium nitrate, 1 g.; 85 per cent formic acid, 3 c.cm.; pure glycerin, 5 c.cm.; acetone, 10 c.cm.; and 95 per cent alcohol, 10 c.cm. It is then washed in distilled water and treated with a solution of 3 drops of saturated alcoholic solution of mastic mixed with 7 c.cm. of 95 per cent alcohol, for 2 minutes. The gum is poured off, and breath blown on the surface of the smear, the slide then being washed in distilled water. The slide is flooded with a 1 per cent aqueous solution of silver nitrate, heated over a burner until bubbles begin to form (not boiled) and kept at this temperature for 3 minutes. The silvering is repeated once, then the silver is poured off, and a thin coating of developing solution applied, and the slide left under electric light for 2 minutes while warmed gently with a flame. The stained slide appears brown. The developing solution consists of hydroquinone, 0.31 g.; sodium sulphite, 0.06 g.; 40 per cent neutral solution of formaldehyde, 2.5 c.cm.; pyridine, 2.5 c.cm.; saturated solution of mastic in 95 per cent alcohol, 2.5 c.cm.; and distilled water 15 c.cm. The slide is then washed in water, dried with filter paper, and examined. The mastic solution should be prepared freshly, but the developing solution keeps from 2 to 3 weeks in a light room, after which the mastic separates and settles to the bottom of the bottle.

MORBID ANATOMY AND PATHOLOGY

Laboratory Tests

Serum Diagnosis

Leiboff has invented a new slide flocculation test. The antigen is prepared from the powder of 6 pooled ox-hearts after extraction 3 times with ether. The alcoholic extract is made with 5 c.cm. of absolute alcohol per gram of powder and is cholesterolized with 6 mg. per c.cm. After solution of the cholesterol and standing for 24 hours it is filtered. One-tenth of the extract is taken to make a saturated solution of dimethylamidoazobenzene, which is filtered and then diluted to 1 in 4 with more alcoholic extract. The remainder of the extract is used to make a saturated solution of sudan III which is then filtered. The two solutions are mixed in the proportion of 85 sudan III to 15 dimethylamidoazobenzene and well shaken. Antigen so prepared had fully retained its properties for 18 months. For the test a volume of antigen is placed in a wide test-tube (15 mm. diameter) and diluted quickly with 2 volumes of 0.9 per cent sodium chloride solution. The tube is closed with a cork covered with tin-foil and shaken rapidly for one minute; the suspension so prepared remains potent for at least 24 hours. In the test proper 2 drops (about 0.08 c.cm.) of inactivated serum are placed on a clean glass slide and one drop (about 0.03 c.cm.) of the antigen suspension is allowed to fall on it from a height of about 1 cm. The mixture is stirred with a thin glass rod and spread to a circle of about 15 mm. diameter after which the slide is rotated by a gyratory motion for 3 minutes. With strongly positive sera large red flocculi appear in a few seconds. After a minute or two of rotation the floccules gather at the edge of the circle, leaving the central portion colourless. With less positive sera the reaction is slower in making its appearance, and with negative ones no flocculation occurs at all. Under a low-power objective the negative mixture is seen to contain large numbers of slender red needle-shaped crystals rather thicker at the centres and pointed at the ends.

Kahn has found that false positive Kahn reactions disappear or are greatly weakened when the test is conducted with reagents maintained throughout at a temperature of 37° C. and conversely are intensified when the test is conducted at 1° C.

Discrepancies in results of syphilitic serum tests.—A good illustration of the wide differences which can occur in the results of tests by what purports to be the same method of a syphilitic serum test was given in a paper by Mahoney and Harrison at the Assembly of Laboratory Directors and Serologists held under the auspices of the Committee on Evaluation of Serodiagnostic Tests for Syphilis and the U.S. Public Health Service, October 21st–22nd, 1938, Hot Springs National Park, Arkansas. The same 34 syphilitic serums tested in 35 laboratories by 'a widely used sero-diagnostic test' gave positive results ranging from 34 fully positive reactions down to 1 positive and 9 doubtful. In another chart the authors showed the differences in results of tests with the same 34 sera in 37 laboratories 'employing test procedures only a few of which conformed to any generally accepted method'. The differences in results were even more striking; at one end of the scale were 9 laboratories which reported from 28 to 34 positive results with the 34 sera, and at the other were 16 which reported from 0 to 9.

The investigations of the committee on evaluation of sero-diagnostic tests for

syphilis have supported those of the League of Nations Health Organization and of the English Ministry of Health in showing the constant need for scrupulous care over technique and for periodical overhaul of methods.

Influence of malaria on the syphilitic serum reactions.—Kitchen *et al.* inoculated 30 persons suffering from psychoses with *Plasmodium vivax* and/or *P. falciparum* and afterwards tested their blood by the Wassermann and Kahn methods. In every case in which malaria developed clinically the serum reactions became positive, 72 per cent of them in the third and fourth weeks after inoculation, and in 60 per cent the reactions remained positive for more than 3 weeks. The highest percentage of positive reactions occurred from 15 to 21 days after the last paroxysm.

Nature of the Wassermann reaction.—Beck has investigated the nature of the Wassermann reaction by parallel tests with heart extract and an extract of a spirochaetal culture (Gachtgens method). The reaction of syphilitic serum was always stronger with the spirochaetal antigen, and in absorption tests the specific Wassermann reagin, as also agglutinins, were removed by the spirochaetal emulsion. The author concluded that the spirochaete of syphilis contains a specific antigen and a lipid which is found also in the extracts commonly used for the Wassermann test. The work supports the view that syphilitic serum reactions are true antibody reactions.

Eagle and Hogan, as a result of similar experiments, conclude '(a) that *T. pallidum* as well as cultured spirochaetes contain an antigenic factor resembling but not necessarily identical with the reactive constituent of tissue extracts and (b) that this factor is only a part of the antigenic complex of the organism'. They explain the stronger reactions given by syphilitic serum with spirochaetal antigen than with organ emulsion on the grounds of the former finding in the syphilitic serum antigen more closely related to it than in the lipid in an organ emulsion. The fact that spirochaetal antigens contain factors not present in tissue lipid antigens suggests that many syphilitic serums may give positive reactions with spirochaetal suspensions but not with tissue lipoids.

Improved method of the Wassermann test.—The conception of the syphilitic serum reaction as a true antibody-antigen reaction has led Richardson to exploit the zone phenomena inherent in such reactions for improvement of the Wassermann test. Working on the Harrison-Wyler method as a basis by using in an additional tube a double quantity of serum with a 10-fold to 15-fold dilution of the usual emulsion, he has largely eliminated the non-specific doubtful reactions and has made the test much more sensitive. The advance may be gauged by the fact that the Harrison-Wyler method has so far proved the most sensitive of any in Great Britain which did not give false positive reactions.

Infectiousness of syphilis.—Frazier and Pian report a case in which a patient was infected with syphilis by transfusion from a donor 20 days before the latter showed a primary sore.

Barnett and Kulchar have investigated by inoculation of rabbits the infectiousness of saliva obtained directly from the parotid duct in 7 cases of untreated secondary syphilis. In no instance was any evidence of syphilis found in the inoculated animals, and the authors conclude that the saliva is infectious in syphilis only when there are lesions in the mouth.

ACQUIRED SYPHILIS

In Children

Smith has collected 125 cases of acquired syphilis in children under 10 years of age. In the Johns Hopkins Hospital in 17 years, 45 cases of early acquired syphilis were seen in children under 11 years of age and 90 in children from 11 to 15. In the same period the hospital dealt with 1,025 cases of congenital syphilis and 4,487 of early syphilis in adults. In the children the modes of infection were attempted sexual intercourse, 43; kissing, 15; household contact, 14; transfusion, 9; no information, 44. Females were infected twice as often as males, mainly as a result of attempted sexual intercourse.

Early Syphilis in a Yaws Case

Rajam has reported a case of early syphilis with primary sore teeming with *S. pallida* and secondary lesions in a native of Cochin aged 39 crippled with tertiary yaws. This case appears to be an important addition to the evidence that yaws and syphilis are not identical and that infection with the one disease does not necessarily confer immunity against the other.

Pyrexia in Early Syphilis

Lemierre has drawn attention to the danger of syphilitic fever in the early stages of the disease leading to a false diagnosis. The fever may be unaccompanied by other external signs, or there may be other signs which are not exactly characteristic of syphilis. Hardly a year passes in which the Hôpital Claude Bernard does not admit a case of chancre of the tonsil. The commonly accompanying fever leads to a suspicion of diphtheria but this can be excluded by easy detachment of the false membrane. A characteristic of value in the diagnosis is that the lesion is unilateral

and accompanied by well-marked submaxillary adenopathy together with the relative mildness of the subjective signs.

Fever in the secondary stage is not so common as in chancre of the tonsil but nevertheless is often a feature of mucous patches of the throat.

Syphilitic Osteomyelitis

Wile and Welton have reported 2 cases of destructive osteomyelitis in early syphilis and believe that the condition is not so rare as has been believed. In the first case, 4 months after appearance of a primary chancre which had been treated with 6 injections of arsphenamine, the patient developed pains in the lumbar region and chest with fever to 102° F. Radiograms showed, in many of the ribs and in the fifth lumbar vertebra and first sacral segment, and also in several dorsal vertebrae, evidence of destructive osteomyelitis suggesting multiple myeloma. In spite of a positive Kahn reaction the syphilitic aetiology of the condition was established only by a biopsy of one rib. Specific treatment resulted in recovery. The second patient had frontal sinusitis and periostitis and osteomyelitis of frontal and parietal bones coincidently with secondary syphilis. The condition rapidly improved under treatment.

Syphilis Cancer

Touraine, pursuing his investigation into the relation of syphilis to cancer, has studied the cases of this nature shown to the French Dermatological Societies from 1920 to 1938 and those published in the *Zentralblatt für Haut- und Geschlechtskrankheiten* for 6 years. As regards the French cases, after exclusions for insufficient details and other reasons, he found that of 88 epitheliomas of the skin, 48.9 per cent had a syphilitic history, and in a further 17.2 per cent syphilis was probable. In 37 cases of cancer of the mouth (12 tongue) including the lips, syphilis was proved in 17 (11 tongue cases) and was probable in 6 (1 tongue). Of 43 cancers of the ano-genital region, syphilis was proved in 24 and probable in 7, making 72.1 per cent.

In the collection from the German periodical were 81 cases, in 55 of which syphilis was proved, and in 1 it was probable.

The treatment of the syphilis in 77 cases analysed from this point of view had been either nil or quite unsatisfactory in all but 3.

Sorba has found further evidence that syphilis predisposes to carcinoma of the cervix uteri. In a hospital in which 1.6 per cent of the patients were syphilitic the incidence of this disease in patients with carcinoma of the cervix was 14.1 per cent. The syphilis rate was not unduly greater than average in cases of carcinoma of other parts of the genital tract.

Syphilis and Tuberculosis

Trail agrees with the view of Dujardin and Dupres that secondary syphilis tends to aggravate tuberculosis and he considers that energetic antisymphilitic treatment is indicated in such cases. On the other hand the late manifestations of syphilis 'have an adverse effect on phthisis, and usually the prognosis of cases with both diseases at this stage of syphilis is benign'. He quotes Gallant's statistics published in 1929 in the *American Review of Tuberculosis* in which it was shown that treatment of the syphilis in 116 tuberculous subjects reduced the mortality to 21.5 per cent, as compared with 57 per cent in 346 untreated tuberculous syphilitics and an average of 26 per cent in the patients resident in the sanatoria studied. In the syphilitic cases treated with antisymphilitic remedies the tuberculosis improved in 51 per cent, which compares with only 20.9 per cent in syphilitic cases in which the syphilis was left untreated. Trail's own experience, in 14 cases observed between 1927 and 1934 and followed up to the time of writing, strongly supported the view that treatment is well worth while. Of 11 group III (Turban-Gerhardt classification) cases, 7 were still alive and 6 of these were known to have had a full course of antisymphilitic treatment. Of 1 the particulars of treatment were unknown, and of the 4 dead, 2 were treated and 2 were not. In the discussion following this paper there was strong support for the view that antisymphilitic treatment is always indicated in tuberculosis.

Influence of Sex Hormones on Course of Syphilis

Hu has added to the evidence already afforded by Kemp and Shaw that the course of syphilis is greatly affected by sex hormones, being inhibited by the ovary. In ovariectomized rabbits the course of syphilis resulting from intravenous inoculation with a large dose of *S. pallida* was more severe than in those with intact ovaries. At the same time he feels that the results of this experiment do not altogether explain the difference between the behaviour of syphilis in females and that in males. Some of his observations suggest that the male sex hormone also plays a part.

CONGENITAL SYPHILIS

Davis gives the following as criteria on the question whether or not the infant of a syphilitic mother should be treated.

- (i) If the mother has received adequate treatment, starting before the fifth month,

treatment of the infant should be withheld pending the development of definite signs. (ii) The histological examination of the placenta is unreliable; 20 per cent of infants of syphilitic mothers with normal placentas prove to be syphilitic and 12 per cent of infants with positive placentas never develop syphilis. (iii) The serum reactions of the cord blood, or of blood from any other part of a new-born infant, are unreliable, being only a reflex of the condition of the mother's blood. The reactions of the infant's blood are not very reliable before the fourth week except for comparison with those obtained later. If at the end of 1 month the reactions are more strongly positive than at 2 weeks, the infant has syphilis. If the blood is negative at 2 weeks, it should be tested every 2 weeks up to 4 months of age and after that every 6 months for 2 years. (iv) A positive result of a dark-ground examination of scrapings of the inner wall of the umbilical vein indicates syphilis but a negative result means nothing. (v) Radiographs of the long bones, if interpreted by an expert, afford valuable guidance. The characteristic changes are a combination of osteochondritis, osteomyelitis, and periostitis. Recent articles, however, 'have shown that non-syphilitic conditions may simulate these separate findings in X-ray so that the interpretation must be done carefully'.

The Little Finger and the Clavicle Signs of Congenital Syphilis

Grafe has investigated a number of cases for the presence of Du Bois's little-finger sign of congenital syphilis. In this, on account of a dystrophy of the middle phalanx of the little finger on one or both sides, this digit is considerably shortened. In the cases attending the Leipzig University Skin Clinic the sign was found in 138 patients, of whom 60 were certainly congenital syphilitics, 50 were probably so, and 28 showed no sign of congenital syphilis. Prior to this the author had found the sign in 55 out of 100 cases of congenital syphilis and in 60 out of 120 which were probably of this nature. Enlargement of the inner end of the clavicle (sign of Higoumenakis) was found in 55 cases, of which 45 were certainly or probably congenital syphilitics, 3 showed no sign, and 7 were not further investigated. Grafe is sceptical of the specificity of this sign.

PROGNOSIS

Aubry *et al.* have analysed the histories of 220 cases of late neurosyphilis (159 general paralysis of the insane, 58 tabes dorsalis, and 3 tabo-paresis) in respect of the treatment they received in the early stages of their infections and found as follows. Of the cases of general paresis, 113 were untreated, 43 had been very indifferently treated, and in only 3 had the treatment been sustained; the details of these 3 cases showed that in only 1 had the treatment been regular. Of the 58 cases of tabes, 42 were untreated, 14 had been treated only slightly, and in only 2 had it been persevered with for some years; in these 2, however, the details show that the treatment had been very irregular. Of the 3 cases of tabo-paresis none had been treated according to satisfactory standards.

Tottie, in an investigation into the earlier history of 141 patients with syphilitic aortitis diagnosed by Moore's criteria, found that only 1.4 per cent had been 'adequately' treated in the earlier stages of the infection and in none of them were the changes marked; only 6 of the 141 had had any arsphenamine treatment.

Harrison, in an article on venereal diseases and life assurance, summarized the results of investigations of 7 groups of authors into the treatment during the earlier stages of their infection of 1,308 cases of cardiovascular syphilis, general paresis, and tabes. The number classed as having been properly treated at first was only 16, and the details of the papers showed that some of these had received no more than 10 injections. The effect of treatment in the early stages in protecting against the late effects of syphilis was illustrated by the figures of the Cooperative Clinical Group, U.S.A., and by changes in mortality rates for general paresis, tabes, and aneurysm and in mean ages at death which had occurred in England and Wales since 1920. As regards the figures of the Cooperative Clinical Group, these showed that in patients treated with not less than 20 arsphenamine injections, with corresponding heavy metal, those found to have developed late manifestations in an observation period of 3 to 10 years were 0.6 per cent symptomatic and 2.6 per cent asymptomatic neurosyphilis, and 1.2 per cent definite and 0.2 per cent possible cardiovascular syphilis. In an observation period of 10 to 20 years the percentages were 1.6 each, symptomatic and asymptomatic neurosyphilis, and 0.0 and 4.9 respectively definite and possible cardiovascular syphilis. By a comparison of results of treatment in respect of muco-cutaneous relapses between the schemes of treatment recommended by the Cooperative Clinical Group and those practised in good clinics in Great Britain the author gave reason for belief that the outlook for well-treated cases in this country was at least as good as that represented by the above figures. As regards rates of mortality from late effects, the author showed that from 1921 to 1937 the crude death-rates per million in England and Wales had changed as follows. In general paresis it fell in males from 69 to 30, and in females from 14 to 12; in tabes it fell in males from 32 to 24, and in females from 6 to 5; but in aneurysm it rose in males from 44 to 51, and in females from 10 to

25. The author suggested that the explanation of the differences between the changes in the rates for males and those for females was partly that the males, being mostly in the Armed Forces during the last war, were better treated during the earlier stages of their infection than were the females (the civilian V.D. treatment arrangements being then only in their infancy) and partly that, after the appearance of signs of a late effect of syphilis, a male is more likely to be treated promptly than is a female. Harrison also showed that in the years 1921 to 1937 the mean ages at death rose in the case of general paresis in males by 4.49 years to 51.0, and in females by 2.6 years to 50.3; in tabes in males by 4.59 years to 61.1, and in females by 2.05 years to 59.8; and in aneurysm in males by 3.83 years to 59.5. On the other hand it fell in females by 2.7 years to 59.3. In the different age periods the steepest falls in mortality from general paralysis of the insane were below the age of 55; and in tabes under 65. The rise in the mortality from aneurysm in males occurred in the age periods after 65; in females it was evident in every age period. Considering that the peak ages of infection are from 20 to 25 and that arsphenamine treatment began to become generalized in Great Britain in 1914, the protective value of modern treatment seems to be manifest in these figures.

Syphilis and Life Insurance

Inquiries by Murrell and Manson into various questions concerning insurance of syphilitic persons in U.S.A. have revealed some interesting facts. In U.S.A. it is calculated that the national incidence of syphilis is about 7 per cent and that of applicants for life insurance about 2 per cent, but inquiries from Life Assurance Corporations show that only 0.127 per cent admit syphilis, so that apparently 16 out of 17 syphilitic applicants either lie or are ignorant of their infection. The companies raise the premium 41.6 per cent for treated primary cases, 57 per cent for untreated primary ones, and 66.6 per cent for untreated secondary. The authors point out that whereas a person who admits syphilis adequately treated from the first and in whom the probability of cure is almost 100 per cent is penalized by a 40 per cent addition to his premiums, the person who denies syphilis, is completely untreated, and in whom the prognosis is much worse, escapes such a penalty.

TREATMENT

Pyretotherapy

A report by Krusen and Elkins on fever therapy by physical means, authorized by the Council on Physical Therapy of the American Medical Association, indicates that in early primary syphilis, a combination of artificial fever therapy and chemotherapy gives better results than either treatment alone. By inducing a body temperature of above 105° F. (40.5° C.) during 10 sessions each of 5 hours, and combining a course of 30 injections of an antisyphilitic drug, cutaneous lesions react promptly and may be free from living spirochaetes after the first fever session. The serological reactions also improve under this treatment.

Combined with Chemotherapy

W. M. Simpson, H. W. Kendell, and D. Rose describe their experiences with artificial fever therapy, which dates from 1931, the apparatus employed being the Kettering hypertherm. Practically from the outset the authors have combined chemotherapy with the fever, and a great advantage of the latter is that it seems to protect the patient against anaphylactoid symptoms if the arsenical remedy is given at the height of the fever. The authors' present system is to give an intramuscular injection of 4 grains of bismuth salicylate at the commencement of the fever sitting, and the arsenical remedy when the temperature has reached 105° F. For the past 4 years (1937-41) the authors have used arsenoxide in a dose of 60 milligrams as the arsenical preparation. Usually one or two sittings are given each week up to 12 sittings. Their results seem to have been better than could have been expected from chemotherapy alone in ocular syphilis and in sero-positive resistant cases of syphilis, and they have been impressed by the possibilities of combined fever-chemotherapy in eradicating early syphilis.

Arsenical Compounds

Stability of Neoarsphenamine

Probey and Harrison have found that in unstable batches of neoarsphenamine the instability is revealed as clearly by exposure for 4 days at a temperature of 70° C. as by heating at 56° C. for 28 days. Of batches with a moisture content of 1.5 to 3.5 per cent, 30 per cent were found to be unstable by this method, but only 8 to 10 per cent of those with a moisture content of less than 1.5 per cent.

Action of Arsphenamine and Bismuth Compounds in vitro

Kast *et al.* found that disodium arsphenamine produced marked or total loss of motility of virulent *S. pallida* in dilutions as high as 1 in 40,960 when in saline and 1 in 20,480 in serum in 15 minutes at room temperature, and in dilutions as high as 1 in 163,840 in 30 to 60 minutes. Neoarsphenamine worked similarly in dilutions of 1 in 20,480 in saline and 1 in 5,120 in serum for 15 minutes, and at 1 in 163,840 when applied for 30 to 60 minutes. Mixtures of neoarsphenamine and virulent

S. pallida in citrated blood in which the dilutions of neoarsphenamine were as high as 1 in 40,960 when injected into rabbits' testicles after standing for 15 minutes at room temperature failed to infect. Human beings were transfused with 300 c.cm. of 1 in 1,000 to 1 in 3,000 neoarsphenamine and with 300 to 400 c.cm. of 1 in 10,000 disodium arsphenamine, all in citrated blood, without ill effect. The authors recommend therefore that if a transfusion donor is suspect, the citrated blood should have mixed with it neoarsphenamine to a strength of 1 in 10,000 (1 c.cm. of a 1 per cent solution per 100 c.cm. blood) and that the mixture stand for 15 minutes at room temperature before being given.

Eagle in previous publications has shown that arsphenamine and bismuth compounds immobilize and kill pathogenic *S. pallida* *in vitro*, the effect being influenced by concentration, duration of exposure, temperature, and the presence of tissue extractives—the last markedly inhibiting the action of these drugs. In order to determine the concentrations which would act in the presence of tissue extractives, he mixed the respective drugs with the fluid oozing from an oedematous chancre in a rabbit and allowed them to act for varying periods. In these conditions arsenoxide had a definite antispirochaetal action within 1 to 2 hours at room temperature (25 to 34° C.) when in dilutions of 1 in 1,000,000 to 1 in 4,000,000; arsphenamine, neoarsphenamine, and silver arsphenamine in dilutions of 1 in 250,000 to 1 in 1,250,000; and two water-soluble compounds of bismuth in dilutions (of bismuth metal) of 1 in 50,000 to 1 in 225,000. If it is calculated that a dose of 0.4 g. arsphenamine when administered to an individual of 70 kg. is diluted in the body to 1 in 100,000, that 0.05 g. arsenoxide is diluted to 1 in 800,000, and that 0.04 g. bismuth metal is diluted to 1 in 1,000,000, it will be seen that the concentrations of the arsenical drugs which are reached in the body after injection of therapeutic doses are higher than those found effective *in vitro*, and the author suggests that the mode of action of the remedies *in vivo* may be similar to that *in vitro*. As regards bismuth, the longer duration of action and the higher temperature at which it acts in the body may explain the disproportion between the therapeutic dose (but 0.04 g. is a very low dose for a man of 70 kg.: the usual weekly dose in Great Britain is 5 or more times as much) and that which is effective *in vitro*. In this connexion the work of Sollmann, Cole, and Henderson indicates that under injections of insoluble compounds of bismuth the concentration of the metal attained in the body varies from 1 in 2,000,000 in the blood to 1 in 30,000 in the kidney. Eagle suggests that even a concentration of 1 in 2,000,000 acting for weeks may be as effective *in vivo* as that found effective *in vitro*.

In an editorial on the above work of Eagle and that of Kast, Peterson, and Kolmer, Moore suggested *inter alia* the testing of different batches of arsphenamine compounds *in vitro* instead of by the usual trypanocidal method. Kolmer *et al.*, investigating this, conducted a number of experiments which resulted in the conclusion that variable factors referable to serum, tissue extractives, temperature, and numbers of spirochaetes exposed to the action of the remedies make the *in vitro* test an unreliable measure of the therapeutic effectiveness of an arsphenamine compound. The details showed that there was no parallelism between the immobilizing dose *in vitro* and the curative dose for rabbit syphilis. In a later paper the same authors arrived at a similar conclusion in respect of the testing of bismuth.

Mapharsen in the Treatment of Syphilis in Pregnancy

Castallo *et al.* treated 116 pregnant women with mapharsen (or mapharside) and bismuth, one injection of each per week, and compared the results with other series differently treated. In patients treated from before the sixth month the results in respect of live births were, with iodobismuthate of quinine, 75 per cent; mapharsen and bismuth salicylate, 83.7 per cent; neoarsphenamine or acetylarsan, 94.6 per cent. The authors concluded that, from these results, mapharsen appeared to be relatively weak in preventing miscarriages and still-births.

Intolerance of Arsphenamine Treatment in Pregnancy

Contrary to a common belief that arsphenamine treatment is well tolerated in pregnancy, Ingraham advances evidence that in this condition women are more susceptible to toxic effects of these compounds. He cites 7 maternal deaths attributable to neoarsphenamine in one locality of Philadelphia since 1931, and a review of side-effects of 6,345 injections given to 733 pregnant women in Philadelphia General Hospital which revealed an incidence of toxic reactions much higher than is encountered in routine work. He quotes cases from the literature in support of his thesis, and they include 35 deaths, to which he adds 7 in his own experience. The 42 included 27 haemorrhagic encephalitis, 4 collapse, 3 parenchymatous degeneration of the liver, 2 dermatitis, 1 eclampsia, 1 aplastic anaemia, and 4 in which the cause of death was unknown. He suggests that the evidence indicates care in initial dosage, and that 'it would possibly be advisable to give more consideration to adequate preparatory heavy metal therapy before commencing active arsenical treatment even though one is confronted with an early infection in late pregnancy'. [The last ten words of this quotation suggest that Ingraham has over-

looked the evidence that only bismuth passes the placenta to the foetus until practically the end of the pregnancy (Vol. XI, p. 598), and that therefore if there is a supposition that the foetus has been infected, bismuth is the remedy of choice.]

Tzanck and Lewi say that in the abundant literature on arsenical encephalopathy, the frequency of this complication in pregnant women is striking.

Paley and Pleshette, in reporting a case of haemorrhagic encephalitis in a pregnant female under treatment for syphilis, remark that 158 cases of this complication of treatment have been reported in the literature since 1911, that rather less than half of them were females, and that over 70 per cent of these were pregnant.

Lowered Capillary Resistance in Arsphenamine Dermatoses

Horne and Scarborough have found by the formation of purpuric spots under the application of a negative pressure to the skin that in cases of erythema and dermatitis due to arsphenamine treatment there is a low capillary resistance, and that it can be raised by the administration of hesperidin.

Bismuth

Sollmann *et al.* propose that, in cases in which arsenical treatment is contra-indicated but it is important to get the syphilitic process quickly under control, both a water-soluble and an insoluble preparation of bismuth be administered for the first 3 weeks, after which the treatment may be continued with the insoluble preparation. In the authors' experiments the soluble preparation was given 3 times in the first week, twice in the second, and once in the third; the insoluble one was given once weekly, and without the aid of the soluble preparation the effective concentration of bismuth in the blood would not have been reached for 2 to 4 weeks. As it was, it was reached within the first 2 weeks.

Oral Administration

Meininger and Barnett have reported on the treatment of syphilis by sobisminol mass, a preparation of bismuth introduced by Hanzlik, Lehman, and Richardson in 1937 for administration by mouth. It is given in capsules each containing 0.2 g. sodium bismuthate, 0.4 g. tri-isopropanolamine, and 0.1 g. each propylene glycol and ethyl alcohol, and the bismuth content of each capsule is 0.15 g. The dosage administered to adults was eventually 1.8 g. a day, but the authors believe that 1.2 g. is optimal. The report is based on 143 patients followed up and 49 more in whom data respecting tolerance were available. The drug was generally well tolerated but sometimes there was some mild gastro-intestinal disturbance. In 33 cases the time required for the remedy to cause disappearance of *S. pallida* from the juice of lesions was investigated, and in 29 it averaged 4.2 days; in the other 4 they had not disappeared at the end of 2 weeks. Lesions cleared up rapidly. A comparison of the results of treatment with sobisminol and neoarsphenamine and those with iodobismitol (a soluble compound of bismuth for intramuscular injection) and neoarsphenamine in respect of reversals of serum reactions and of eventual state of the spinal fluid was favourable to sobisminol, but several patients relapsed under treatment, 8 out of 74 clinically and 1 serologically under sobisminol and 4 clinically and 5 serologically under iodobismitol. [In both series this seems a high relapse rate.]

Scholtz *et al.* reported on early and late cases of syphilis treated with sobisminol mass. In regard to disappearance of *S. pallida* and involution of lesions their results seem similar to those of Meininger and Barnett but no serological results are given. Results in respect of relief of pains in tabes dorsalis appear to have been good.

Deposit in Bones

Whitridge has reported the results of radiographic examinations of the infants of 72 non-syphilitic women treated during the last 3 months of their pregnancies with bismuth injections (1 c.cm. of a suspension of bismuth salicylate containing 0.1 g. metallic bismuth) weekly to a total of 8 in 6 cases, 7 in 5, and 3 in 1. The infants were all X-rayed in the first week of life, and 9 showed definite changes at the ends of the long bones similar to those described by Caffey in infants born of syphilitic mothers treated with bismuth during their pregnancies and in the ends of the bones of growing dogs after bismuth injections. The changes consisted of areas of increased density, and the slight question of their being due to syphilitic osteochondritis which arose in Caffey's cases was excluded by the fact that the mothers and infants were non-syphilitic. One infant died, and microscopical examination of certain epiphyses showed them to be normal at the junction with the shaft except for an excess of calcified matrix which extended 1 mm. down the shaft as a dense zone. Chemical tests for bismuth were negative but the author concludes that Caffey's assumption that the changes were produced by bismuth is correct.

Toxic Effects of Bismuth

Cervico-vaginitis due to bismuth poisoning.—Simon recalls that in collaboration with Bralez, Durel, and Pereton he published a very severe case of diphtheroid ulceration of the cervix and vagina resulting from bismuth poisoning. The distinguishing characteristic after removal of the false membrane was a number of blue or black points and patches such as are seen in the mouth in bismuth poisoning. He now reports a case of ulceration of the vagina which puzzled a number of venereo-

logists of repute, until one of them who had seen Simon's first case drew attention to some characteristic black spots due to deposition of bismuth sulphide in the capillaries. Ulceration results from blockage of vessels and consequent necrosis.

Routine Courses

In correspondence in the *British Medical Journal* on the treatment of syphilis Batchelor and Lees expressed the view that the concurrent intermittent system constitutes the most intensive attack on the organism. Their unit course consists of 4 injections of '914' in the first 2 weeks, totalling 1.35 g., followed by 8 \times 0.6 g. at weekly intervals, all this concurrently with 10 intramuscular injections of an insoluble preparation of bismuth (Injectio Bismuthi B.P. 1 \times 0.2 g. Bi metal and 9 \times 0.3 g.) at weekly intervals. A minimum of 4 such courses is given if the first is followed by negative serum reactions, the interval between any 2 courses being 4 weeks. In 675 male cases of early syphilis, this course has been followed by relapses in no more than 0.9 per cent.

Wilkie recommends 2 \times 0.45 g. neoarsphenamine in the first week, followed by 9 \times 0.6 g. at weekly intervals, all concurrently with 10 \times 0.24 g. Bi. Four such courses are recommended and Wilkie claims for them 100 per cent cures.

Clarke has published a useful summary of the present position in regard to the so-called 5-day treatment of syphilis. In 1933 Chargin in collaboration with Leifer and Hyman began to treat selected cases of early syphilis by an intravenous drip method in which 0.1 g. neoarsphenamine is administered per hour for 10 to 15 hours a day for 4 to 5 days, the total dose being 4 to 5 g. Up to the time of writing 86 cases had been treated, with satisfactory results in 83 per cent (counting 7 untraced patients as failures). On account of the frequency of toxic reactions, including one death from encephalitis, mapharsen had been substituted for neoarsphenamine and 300 cases treated with it. The toxic reactions had been fewer with mapharsen and therapeutic results appear to have been so far as good as with neoarsphenamine. Cormia, however, reporting at a conference on this form of treatment held in New York, apparently early in May 1940, said that in the 300 cases there had been 6 cases of encephalitis, with 2 deaths. This, he said, was about 5 times the rate which would be expected in conventional therapy. One would say that it was a large multiple of 5 times the rate under conventional therapy. [As regards the relative efficacy of mapharside as compared with neoarsphenamine, in a recent symposium on the massive arsenotherapy of early syphilis, by Baehr *et al.*, it was shown that results comparable with those following the use of neoarsphenamine by this method of administration were obtained with mapharside only when its total dose was raised to 1,200 mg., or nearly one-third that of neoarsphenamine. In ordinary methods of administration the single dose of mapharside is commonly one-tenth that of neoarsphenamine; such a dose is likely to be far less effective than the usual dose of neoarsphenamine, and the experience of Castallo *et al.* in the prevention of congenital syphilis, reviewed above, supports this.]

The Cautery in Syphilis

Gougerot regrets that the use of the cautery has been abandoned in dermatosyphilography. After quoting 3 cases in his experience in the past in which eczema alternating with asthma and other troubles were cured by the application of the cautery and tended to reappear when the cautery burns healed, he reports 3 in which various troubles were held at bay by fistulas resulting from bismuth abscesses, the bismuth having been given for the treatment of syphilis. He thinks that in these cases the bismuth fistulas played the role of a cautery. In the first a chronic eczema and asthma cleared up and remained well whilst a bismuth fistula remained open and returned when the fistula was removed by operation. In the second case a patient with syphilitic aortitis had angina pectoris which was aggravated by antisyphilitic treatment but was completely relieved from the first opening of a bismuth fistula and during its continuance for 2 years; 3 weeks after removal of the fistula the angina returned. It disappeared again when the cautery was applied and reappeared when the burns healed. Gougerot explains the resistance of this case to antisyphilitic treatment on the grounds of the angina being due to cicatricial contraction, and he offers the same explanation of a case of tabes with very severe lightning pains which were aggravated by antisyphilitic treatment but relieved by a bismuth fistula and returned when this was cured; in this case also the cautery afforded complete relief.

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TALIPES

See Surveys and Abstracts 1939, p. 558.

TAPEWORM INFECTIONS, INTESTINAL

See also Surveys and Abstracts 1939, p. 558.

DIPHYLLOBOTHRIUM LATUM**Symptoms**

Tötterman has described the anaemia which accompanies this infestation as an

1468, 1469

1470

KEY NUMBERS

1470

erythropoiesis in the marrow with normoblasts and a slight shift to the left in the nuclear index of the neutrophils. When the anaemia is hypochromic the number of normoblasts is not raised and generally the eosinophils are slightly increased. But when the anaemia is of the pernicious type the bone marrow shows an increased erythropoiesis with more megaloblasts and premegaloblasts.

HYMENOLEPIS NANA

Treatment

1473

Maplestone and Mukerji state that gentian violet is a valuable drug for the treatment of *H. nana* infection and possibly the only one of any real value. More work is needed to decide whether a course of treatment for a week or longer, or several courses of 3 days' duration at weekly intervals, will prove the best. The interrupted form of treatment instead of a continuous course of 6 or 7 days was tried in an effort to avoid the nausea and vomiting. The gentian violet was always given in hard gelatin capsules. An interval of 1 month or longer should pass before the absence of infection can be concluded. The adult dose is 1 grain 3 times a day for varying periods, according to circumstances.

Ocular Sparganosis

Joyeux reports that sparganum infection of the eye is becoming steadily commoner in the Tonkin delta. Poultices are made from the tree frog *Rana limnocharis*; the emptied abdominal cavity is applied to the eye, or the flesh of the thighs is chopped up to make a poultice. This practice is based upon the popular belief that conjunctivitis is due to worms and that these frogs feed upon them, and that the exudation of the batrachian cures oedema and ascites. The sparganum may settle on the lids, may penetrate the orbital fat, or may burrow towards the surface, the face, temple, or region of the cheek. At first the lids are inflamed, and if they are opened pieces of the parasite are apt to be left behind; but when the worm is encapsuled by tissue reaction, removal is relatively easy.

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Maplestone, P. A., and Mukerji, A. K. (1939) *Indian med. Gaz.*, **74**, 195.

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TESTIS AND CORD DISEASES

1475-1479

See Surveys and Abstracts 1939, p. 559; 1940, p. 550; 1941-2, p. 405.

TESTIS, UNDESCENDED

See also Surveys and Abstracts 1939, p. 561; 1940, pp. 14 and 551; 1941-2, pp. 5 and 406.

TREATMENT

1480

Testosterone propionate.—Testosterone propionate has been increasingly employed of late in the treatment of hypogonadism due to cryptorchidism and the consensus of opinion is that it constitutes an effective substitution therapy. Kearns, for example, investigated its use in castrates and in cryptorchids. The usual dosage he employed was 10 mg. twice weekly, but in 2 out of 6 cases 5 mg. twice weekly was sufficient to produce and maintain increased strength and endurance, and a desire to expand their work. There also appeared libido, erections, ejaculations, ability for coitus, and an increase in the growth of the beard. After 3 to 6 weeks the prostate was found to have regenerated perceptibly and in from 6 to 8 months it approached its normal size. The author also found that testosterone in the form of an ointment (2 mg. of testosterone in each c.cm.) gave excellent results, at least equal to those obtained with injections. A total average weekly dose administered to castrates was 20 mg. by injection and 28 mg. by inunction. Patients were directed to rub in the ointment vigorously for 20 minutes at bedtime into a hairless region of the skin, preferably on the anterior abdomen.

Kearns, W. M. (1939) *J. Amer. med. Ass.*, **112**, 2255.

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TETANUS

See also Surveys and Abstracts 1939, p. 562; 1940, pp. 10, 137, and 552; 1941-2, p. 406.

COURSE AND PROGNOSIS

1481

Cole discusses the prognosis of tetanus, based on an analysis of 43 consecutive civilian cases receiving approximately the same method of treatment, which consisted essentially of large doses of antitoxin given immediately after diagnosis, usually by the intravenous route. In most cases the dose was a single intravenous injection of 200,000 international units of antitoxin, but in a few mild cases was reduced to 100,000 I.U. The wound was not touched for 1 hour and then surgical manipulation was limited to the minimum needed to ensure free drainage and for irrigation with hydrogen peroxide.

The prognosis was best between the ages of 5 and 20 years and worst over 60 years. Good general health is very important. Diseases of the heart and lungs increase the risk of terminal pneumonia. The prognosis was better in females than in males, probably because their wounds were slighter and are kept cleaner. The

more severe the wound the more severe is the tetanus as a rule, and the amount of deep sepsis is important in determining the prognosis. The prognosis is best in wounds of the lower limb, and wounds on the upper limb and face are most dangerous.

An incubation period less than 7 days usually indicates a fatal issue, and one of more than 14 days a good prognosis, but an incubation period between 7 and 14 days gives no indication of the prognosis. A better guide to prognosis is given by the length of time elapsing between the first symptom of the disease and the onset of reflex spasms. The appearance of reflex spasms within 48 hours of the onset indicates that a lethal dose has been absorbed. Administration of antitoxin at the earliest possible moment is important; it should be given on suspicion and not delayed until confirmation of the diagnosis. In the absence of a septic wound which is not draining, antitoxin may be discontinued as soon as the reflex spasms cease.

TREATMENT

Prophylactic

Sulphonamide Drugs

Mayer published a preliminary note on the experimental production of antitetanic prophylaxis in mice by the sulphonamide derivatives, sulphanilamide and sulphapyridine (M & B 693). Mice injected with earth containing tetanus bacilli in suspension usually died with tetanus 3 or 4 days later; of 30 mice, 1, or 3.5 per cent, recovered. Out of 95 mice to which the sulphonamide derivative was given by mouth at the same time as the injection of tetanus bacilli, 41, or 43 per cent, escaped tetanus. Of the 2 sulphonamide derivatives, sulphapyridine had the advantage that, though less potent, it was less toxic.

Active Immunization

Ramon drew attention to the complete success which has attended the use in France of active prophylaxis against tetanus in humans and in domestic animals. The method, first tried in 1923 and used ever since, was based on the use of tetanus antitoxin by subcutaneous administration. The technique evolved in the last 10 years, which has been found completely satisfactory, was the subcutaneous injection at intervals of 2, or preferably 3, weeks of 1, 2, and 2 c.cm. of antitoxin. A final dose of 2 c.cm. one year later was recommended to ensure complete and durable immunity. This method was of the greatest importance for communities of people, such as soldiers, school children, and miners, in whom tetanus might occur; by its use tetanus is completely banned. Moreover, the French Army has vaccinated its horses for 10 years, with the result that there has been no further case of horse-tetanus in France. Another advantage of the method is that it can be given together with antidiphtheritic or other prophylactics.

Prevention is all-important. All septic wounds which cannot be drained or contain foreign bodies should receive 3,000–5,000 units of antitoxin on alternate days for 3 doses and then weekly doses until clean. An injection should be given before operating on old wounds.

Boyd describes the offering to the regular troops in 1938 of active preventive immunization against tetanus following the lines already suggested by Ramon. Since then this form of prophylaxis has been standardized both in the British Army and the R.A.F. The toxoid used is tetanus toxin treated at 37° C. with weak formalin. The initial dose given subcutaneously is 1 c.cm. followed in 3 or 4 weeks by 1.5 c.cm. and a fortnight later by a third dose of 1.5 c.cm. This series may result in very prolonged immunity and causes no reaction. In any case 2 doses of 1 c.cm. at 6 weeks' interval are found to raise the level of tetanus antitoxin in the recipient's blood to about 0.5 unit per c.cm., a level sufficiently high to prevent an attack of tetanus. With only 2 doses it may be necessary to repeat immunization after a 5-year interval.

In wounded, but unvaccinated, soldiers the French authorities recommended as initial treatment 1 c.cm. of tetanus toxoid and 3,000 units of antitoxin, and then at 15-day intervals 2 further doses of 1 c.cm. of toxoid (Ramon). This represents production of active immunity during a period of temporary protection by the antitoxin. Much larger doses of antitoxin may be considered necessary, e.g. a total of 150,000 units while the toxoid is being given, but the important point is that the combined methods have given good results in French hands.

Recommendations by the Medical Research Council.—Early in 1939 the Medical Research Council arranged for the provision and supply of tetanus antitoxin in the event of war and made recommendations as to dosage. The prophylactic dose is 3,000 international units (I.U.), equivalent to 1,500 American units (A.U.), and is contained in a volume not exceeding 3 c.cm. During the early part of the 1914–18 war a dose of 500 A.U. was administered as a routine, and the effect on the case-incidence of tetanus was dramatic before the end of 1914; the tendency since then has been to advocate the administration of 1,000 and more recently of 1,500 A.U. The dose to be administered for prophylaxis, in case tetanus antitoxin is again

required, has accordingly been fixed at 3,000 I.U.; this can be increased or repeated if necessary. The ampoules of concentrated antitoxin required for the treatment of cases of tetanus contain not less than 20,000 I.U. in a volume not exceeding 8 c.cm.

The relation of the A.U. to the I.U. is 1 : 2, but in order to avoid confusion the strength of tetanus antitoxin is expressed in both units.

Immunization in the Forces.—H. J. Bensted advises that in addition to immunization with two doses of plain formol toxoid, all wounded should receive a single dose of 3,000 units of tetanus antitoxin as soon as possible; and if they have not been previously immunized he recommends 2 subsequent doses of antitoxin of the same size to be given with a week between. Among the Dunkirk casualties 8 cases of tetanus were reported, all occurring in unprotected troops. There were no cases among those who had been actively immunized.

Bensted, H. J. (1940) *Lancet*, 2, 788.

Boyd, J. S. K. (1938) *J. R. Army med. Cps*, 70, 289.

Cole, L. (1940) *Lancet*, 1, 164.

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Ramon, G. (1939) *Pr. méd.*, 47, 877, 981.

THROMBOSIS OF CEREBRAL VEINS AND SINUSES

1482 See Surveys and Abstracts 1941-2, pp. 92 and 407.

TONSILS DISEASES

1484-1488 See Surveys and Abstracts 1939, p. 563; 1940, p. 553; 1941-2, pp. 60 and 408.

TOXICOLOGY: I.—HOMICIDAL, SUICIDAL, AND ACCIDENTAL POISONING

See also Surveys and Abstracts 1939, p. 565; 1940, p. 554; 1941-2, p. 408.

SYNTHETIC ORGANIC SUBSTANCES

Cyclic Ureides and Barbituric Acid

1496

Treatment.—As a result of favourable results obtained in animal tests, picrotoxin has been tried clinically in barbiturate poisoning. Before using this drug it is important to make a certain diagnosis of the cause of the patient's condition, as there is definite evidence that the drug is dangerous in cases of morphine poisoning.

The dose of picrotoxin is 0.5 to 2 mg. and there is a very narrow margin of safety. In barbiturate poisoning, however, much higher doses can be used. The drug must be given in divided doses of 3 to 10 mg. Overdosage must be avoided, since a convulsive attack is followed by increased depression. In most of the reported cases the drug had been given intravenously during the first stages of the treatment, at intervals of 20 minutes to an hour until the patient responded. Since picrotoxin is detoxicated fairly rapidly in the body, to be effective the amount present in the blood must be maintained. As the patient improves the intramuscular route may be employed.

Experimental tests reported by Bleckwenn *et al.* (1937) showed that 1 mg. of picrotoxin was an antidote for 30 to 40 mg. of pentobarbital sodium, sodium amytal, or their thio derivatives. Bleckwenn and Masten later (1938) reported on the use of picrotoxin in 6 patients poisoned with barbiturates taken with suicidal intent. They recommend for an emergency treatment administration of picrotoxin intravenously in a 1 in 1,000 solution at a rate of 1 c.cm. per minute until pupillary and corneal reflexes return, and subsequently subcutaneous administration. The total amount administered to each of 5 patients who recovered varied from 24 mg. to 148 mg.; 669 mg. were administered to one patient who died, and it was considered this was probably more than was necessary.

The dose of barbiturate which had been taken was not always known, and the recovery of some of the drug by gastric lavage reduced the amount absorbed; the time that had elapsed since taking the drug was also a factor causing variation in the amount of antidote required. The cases reported by Bleckwenn and Masten received the following dosage. (i) 24 mg. picrotoxin; patient confessed to having taken 8 capsules each of 3 gr. of sodium amytal. (ii) 669 mg. picrotoxin; it was estimated that the patient had taken 75 gr. of sodium amytal and 18 gr. of pentobarbital sodium; patient died. (iii) 68 mg. picrotoxin. (iv) 148 mg. picrotoxin; patient had taken 156 gr. of sodium amytal. (v) 60 mg. picrotoxin; patient had taken 80 gr. of sodium amytal and 6 gr. of phenobarbital. (vi) 30 mg. picrotoxin; patient had taken 120 gr. of sodium amytal. As additional measures to counteract the narcosis, they recommended gastric lavage, and purgation (magnesium sulphate not recommended), continuous oxygen, promotion of diuresis by parenteral fluids and intravenous sucrose, and the oral administration of dextrose to prevent acidosis.

Bleckwenn, W. J., and Masten, M. G. (1938) *J. Amer. med. Ass.*, 111, 504.

— — and Tatum, A. L. (1937) *J. Pharmacol.*, 60, 99.

TOXICOLOGY: II.—INDUSTRIAL POISONING

See also Surveys and Abstracts 1939, p. 570; 1940, p. 559; 1941-2, p. 411.

NITRO- AND AMINO-DERIVATIVES**Tetryl**

Leigh-Silver, of the Royal Arsenal, Woolwich, writing on the diseases which occur in filling factories, describes poisoning by tetryl. Tetryl (trinitrophenyl-methylnitramine) causes yellow staining of the hands of workers in 1 to 3 days and of the face and scalp in 1 to 3 weeks; sunlight deepens the colour. It does not cause constitutional symptoms but, unless precautions are taken, is a potent source of dermatitis, though susceptibility varies greatly. Tetryl irritation may release an attack of chronic skin disease. The rash generally affects the face first, especially the sides of the nose, and around the eyes and the corner of the mouth; it is intensely irritable. Later the condition spreads to the chin, neck, and back of the head, and may lead to a papular eruption. There are no characteristic changes in the blood.

1536

Prophylaxis

Protective clothing should be provided. Shops should be well ventilated, and the atmosphere dry. Great care should be taken to avoid raising dust. The hands should be washed thoroughly in running water before the face is washed. The addition of 5 per cent sodium sulphite will assist removal of tetryl by converting it into a soluble substance. Workers should be warned against the use of proprietary ointments. A water-soluble skin varnish should be used on the face and arms before beginning work. Susceptible persons should be removed from contact with the substance; convalescents are particularly susceptible.

Treatment

Oils and ointments aggravate the condition, but a soothing lotion, such as calamine lotion, should be applied. After the acute inflammation has subsided the affected parts may be cleansed with olive oil. Workers who recover from an acute attack in less than a fortnight may be allowed to resume contact work after a further week. Legally these cases are entitled to compensation for the period of disability.

Leigh-Silver, A. L. (1938) *J. R. Army med. Cps*, **71**, 87.

TRACHEA DISEASES

See Surveys and Abstracts 1939, p. 573; 1940, p. 563; 1941-2, p. 412.

1541-1544

TRACHOMA

See also Surveys and Abstracts 1939, p. 573; 1940, p. 564; 1941-2, p. 412.

Errata.—In Vol. XII, p. 218, last paragraph, 1st line, and p. 219, top line, for 'lid' read 'lip'—as follows: p. 218 'The lower lip' . . .; and p. 219 'The wound in the lip' . . .

1545

TRACHOMA IN ENGLAND

Trachomatous conjunctivitis has been recognized in England more often during 1940 and 1941 than previously. This is partly due to the influx of infected Jews from Europe, and partly to the recognition of the disease in a slight form resulting from examination of the conjunctiva and cornea by modern methods. Every case of chronic conjunctivitis, the cause of which cannot be determined, and which resists ordinary treatment for three months, should be carefully examined with the slit lamp for the signs of trachoma; examination under focal illumination with the corneal loupe is insufficient. Papillary hypertrophy may be present in any form of conjunctivitis, even in that due to a mere erosion of the lower lid. Translucent bleb-like excrescences of the conjunctiva or generalized subepithelial oedema and also increasing vascular network of the conjunctival limbus on to the upper fifth of the normally clear cornea, together with recognition of virus-inclusion bodies in scrapings of the conjunctival epithelium which have been stained for 24 hours in Giemsa solution, leave no doubt as to the diagnosis of trachoma.

It cannot be too strongly insisted on that a person of good social position may be examined and found to be infected with trachoma, although it may be stated that no ocular disability has been experienced. This is especially the case with Jews from Austria and Czechoslovakia.

TREATMENT

The treatment of trachoma by certain drugs or caustics described in Vol. XII, pp. 216 and 217, requires some revision in the light of recent experience in England; that described may be used for Egyptian labourers but is too painful for use in Great Britain. Prophylactic collyria may contain zinc sulphate or chloride, 0.125 per cent, solution of chloramine-T, 0.25 per cent, or eusol, 10 per cent. When silver nitrate solution is used in early cases some preliminary anaesthesia with a solution of cocaine hydrochloride, 2 per cent, should be used; the strength of the salt should be 1 per cent. After the painting the conjunctival sac should be irrigated with normal saline solution. Massage with 0.25 per cent mercuric chloride cannot be endured by sensitive people. Massage with chaulmoogra oil, radiotherapy, and

high frequency currents are probably without benefit for the trachoma itself, although in some cases the patient experiences relief. This is also the case with the derivatives of the sulphonamides. This statement is made as the result of experience and is contrary to the opinion of some American and Continental therapists (A. F. MacCallan). After mechanical treatment, as described in Vol. XII, p. 217, the use of massage with mercuric chloride, 1:500, is unnecessary and too painful. A collyrium of copper sulphate, 1 per cent, is too painful and the copper stick should seldom be used in Great Britain. MacCallan recommends a collyrium composed of zinc sulphate, mercuric chloride, and methyl violet in 50 per cent strength: it is difficult to make up so as to remain unaltered for a long period, and a solution of chloramine-T, 0.25 per cent, is probably nearly as good for prolonged use. In all cases in which the upper fornical conjunctiva is smooth, MacCallan recommends the performance of combined excision of tarsus and conjunctiva or tarsectomy. This is a difficult operation which, however, should be within the scope of any skilled ophthalmic surgeon.

Sulphanilamide.—P. Richards *et al.* employed sulphanilamide in 12 Indian children all of whom showed trachoma with follicular atrophy and pannus. Striking improvement occurred in all cases, and after 4½ months the conjunctivae in each case had become smooth and free from follicles. Corneal infiltrates disappeared in all eyes except one, and the corneal activity was apparently checked. In 2 untreated children, used as controls, there was no apparent improvement during the period of observation, but improvement rapidly occurred when sulphanilamide was given later. Sulphanilamide therapy effected the disappearance of the epithelial-cell inclusion bodies characteristic of active trachoma.

MacCallan, A. F. (1941) (Personal communication) *Trachoma in England*.

Richards, P., Forster, W. G., and Thygeson, P. (1939) *Arch. Ophthalm.*, N.Y., 21, 577.

TRENCH FEVER

See Surveys and Abstracts 1939, p. 574.

1548

TRICHINIASIS

See also Surveys and Abstracts 1939, p. 575; 1941-2, pp. 90 and 412.

AETIOLOGY

1549

The incidence of trichiniasis in the United States of America has recently been shown to be much higher than formerly suspected. S. E. Gould found 93 cases in 500 consecutive post-mortem examinations in Michigan. He paid special attention to the pectoral muscles and the diaphragm by the method of digestion with artificial gastric juice. In England an outbreak of trichiniasis was reported in Wolverhampton. Eighty cases were notified and were all among the artisan class in the proportion of 4 women to 1 man. The source of infection was sausage meat which is eaten raw, spread on bread as a meat paste, which the women much appreciate.

CLINICAL PICTURE

McNaught has drawn attention to 'splinter haemorrhages', beneath the nails of patients during the migrating stages of trichiniasis. These are found under the finger and toe nails in 60 to 70 per cent of patients in the active stage of infection.

Evers reported the case of a man, aged 25, admitted to hospital in coma with a history of a rash consisting of small red spots surrounded by larger red blotches; these disappeared after the application of a simple soothing lotion. Neuro-retinitis was present, and the cerebrospinal fluid contained motile trichinella larvae. The blood showed 38 per cent of eosinophils. Recovery took place.

Of 24 collected cases with the larvae in the cerebrospinal fluid, 4 proved fatal; but the presence of larvae in the cerebrospinal fluid was not always accompanied by clinical symptoms. In 15 cases there were signs of encephalitis, such as delirium, stupor, or coma, and often loss of the deep reflexes. In 8 cases meningitis had occurred.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Preparation of antigen.—Bozicevich has described the preparation of diagnostic antigen. Special care is taken to obtain trichinella larvae from digested infected meat free from protein. The dried ground larvae are extracted into neutral 0.85 per cent solution of sodium chloride. No preservative is added, but the vials are subjected to fractional sterilization. This antigen shows no loss of titre after 6 months and may be used for both precipitin and intradermal tests.

TREATMENT

During a search for specific therapeutic treatment in experimental trichiniasis, McNaught *et al.* found that a relatively large amount of sulphanilamide, given over a period of 6 weeks, reduced the number of trichinella encysting in the muscles of rats by 55 per cent. The continuous administration of phenothiazine, in

a dose of approximately one-tenth of the former, over a period of 6 weeks, reduced the severity of trichina infection by 74 per cent.

Bozicevich, J. (1938) *Publ. Hlth Rep. Wash.*, **53**, 2130.

Editorial (1941) *Lancet*, **1**, 182.

Evers, L. B. (1939) *Arch. intern. Med.*, **63**, 949.

Gould, S. E. (1940) *Amer. J. clin. Path.*, **5**, 431.

McNaught, J. B. (1939) *Amer. J. trop. Med.*, **19**, 181.

— Beard, R. R., and DeEds, F. (1939) *Proc. Soc. exp. Biol. N.Y.*, **41**, 17.

TROPICAL DISEASES, GENERAL SURVEY

See Surveys and Abstracts 1939, p. 576; 1941-2, p. 96.

1550, 1551

TROPICAL ULCER

See Surveys and Abstracts 1940, p. 565; 1941-2, p. 413.

1552

TRYPANOSOMIASIS

See Surveys and Abstracts 1939, p. 576; 1940, p. 78; 1941-2, pp. 100 and 413.

1553

TUBERCULOSIS

See also Surveys and Abstracts 1939, pp. 39 and 577; 1940, pp. 94 and 566; 1941-2, pp. 13, 71 and 414.

EPIDEMIOLOGY

Age

Senile tuberculosis is receiving more attention now than formerly. W. E. Snell reported an investigation on 145 male patients of 60 years and over, treated since 1933. The figures indicated that the disease was probably acquired either as a result of a massive re-infection or of numerous re-infections. Cases showing complications were strikingly rare. Specialized forms of collapse therapy were not of great value, and although the majority of patients responded very well when under routine sanatorium treatment as regards their general condition, the local disease of the lungs was uninfluenced, and the majority remained sputum positive.

1554

MORBID ANATOMY

Tuberculous Pericarditis

H. Hannesson surveyed the reported cases of tuberculous pericarditis. Two groups are recognized, (1) in which pericarditis is the most important factor in a clinical picture of tuberculosis, and (2) the extensive disseminated infection. The condition occurs most often in males over forty and in coloured races more often than in the white races. The prognosis is bad, the mortality in two series cited being 83 per cent in both instances.

DIAGNOSIS

X-Rays

F. G. Chandler lays stress on the point that far too much reliance is still placed on physical signs in the diagnosis of pulmonary tuberculosis, and strongly advocates X-ray examination as a routine. He points out, however, that the shadow pattern should be interpreted in correlation with the clinical and especially the bacteriological findings in the case. For example, a carcinoma of the upper lobe, with an incipient atelectasis, may simulate almost exactly a tuberculous infiltration with a small interlobar effusion.

PREVENTION

Tuberculosis and the World War

E. L. Collis surveyed the mortality in the war of 1914-18 with some of the lessons involved. Before 1914 the mortality was declining: during the war there was a steady increase in mortality in all ages up to 30. It was noted further that amongst the females the rise could be correlated with employment in munitions. It did not occur in non-munition areas. In the present war the migrations of tuberculous patients have ebbed and flowed with that of others. Three other factors have operated with that of migration: (1) the evacuation of sanatorium beds in defence areas and of hospital beds for the tuberculous in heavily bombed towns; (2) the congregation of ambulant cases in the shelters; (3) the difficulty in maintaining regular refills for artificial pneumothorax cases. The crux of the problem is as usual the control of the sputum-positive patient who, always a danger to his fellows, may be a serious menace at home, in billets, and in shelters. Mass radiography has not so far been adopted by the British authorities, and A. D. Leigh considers that unless it is adopted, 0.5 to 2 per cent of persons with latent tuberculosis will find their way into the Army.

Chandler, F. G. (1940) *Lancet*, **1**, 1035 and 1071.

Collis, E. L. (1940) *Tubercle, Lond.*, **21**, Aug.-Sept., Supp.

Hannesson, H. (1941) *Tubercle, Lond.*, **22**, 79.

Leigh, A. D. (1941) *Tubercle, Lond.*, **22**, 121.

Snell, W. E. (1941) *Tubercle, Lond.*, **22**, 111.

TUBERCULOSIS, GENERALIZED

1555 See Surveys and Abstracts 1939, p. 582.

TULARAEMIA

1556 See Surveys and Abstracts 1939, p. 582; 1940, p. 569; 1941-2, p. 415.

TUMOURS

1557 See Surveys and Abstracts 1939, p. 583; 1940, p. 569; 1941-2, p. 416.

TYPHUS FEVERS

See also Surveys and Abstracts 1939, p. 583; 1940, pp. 76 and 570; 1941-2, pp. 98 and 416.

EPIDEMIC OR LOUSE-BORNE TYPHUS FEVER

Treatment

Preventive

1559 The most important recent work on this disease has been directed towards the discovery of a satisfactory method of protective inoculation. Murgatroyd has given a comprehensive summary of the various methods which have been tried, and this should be consulted by all who are interested in the subject.

The procedure which holds out the greatest promise of success in peace and war is that of Durand and Giroud. This is based on the discovery that white mice inoculated through the respiratory passages with highly virulent cultures of *Rickettsia prowazeki* develop a massive pneumonia, and their lungs contain enormous numbers of the *Rickettsia* bodies. The emulsified lungs are subjected to differential centrifugalization so as to obtain a fluid which is heavily loaded with the parasites. This fluid is treated with formol and used as a vaccine. The Weil-Felix reaction becomes positive in persons who have been inoculated and presumably a high degree of protection is established.

War Typhus

Danielopolu *et al.* have presented an important report on this subject. They point out that severe hypertoxic forms of the disease are much more common in war-time epidemics than in those occurring in times of peace. The incubation period is uniformly short, about 8 days, which the authors regard as the minimum for this disease. Owing to the rapid passage of the infection through susceptible persons the virulence of the parasites becomes greatly exalted, corresponding to the *virus fixe* of rabies. A high leucocyte count of more than 20,000 is of bad omen, especially if the count continues to rise after the temperature has fallen.

Remarkable results were obtained from intravenous injections of a solution containing 0.5 g. of chlorine and 6.5 g. of sodium chloride in 1,000 c.cm. of water. The dose was 500 c.cm. given *very slowly* once or twice daily. The treatment is reserved for the severe types of case, in which the mortality has been reduced in a very striking degree.

NON-EPIDEMIC OR EPIZOOTIC TYPHUS FEVERS

Tick-Typhus

Q Fever

1560 This disease is related to tick-typhus in being a typhus-like fever conveyed from rodents to man by a tick and caused by a *Rickettsia* body. It was first described by E. H. Derrick in 1937 as a new disease occurring in workers in a large meat factory in Brisbane. About 20 cases without any deaths occurred among 800 employees between 1933 and 1937. The disease lasted from 7 to 24 days, but only one out of 9 patients had a definite rash. F. M. Burnet isolated a filter-passing *Rickettsia* body from experimental monkeys, mice, and guinea-pigs. The virus, called *R. burneti*, is agglutinated by the serum of patients but not by the serum from cases of the other fevers of the typhus group. The disease does not protect animals from attacks of the other typhus fevers, and there is no agglutination of *B. proteus* OX 19, OX K, or OX 2. Bandicoot rats are believed to form the chief animal reservoir of infection in Australia, and a tick, *Haemophysalis humerosa*, is the vector in animals. A virus which is apparently identical was isolated from ticks (*Dermacentor andersoni*) by Davis and Cox in America in 1935; this was called *Rickettsia diaporica* because of its filter-passing properties. Only one human case, in a laboratory worker, has been reported from America. Q fever does not seem to be of much importance as a human disease but is of great interest as a new form of tick-borne typhus-like fever.

Danielopolu, D., Lupu, N. G., Craciun, E., and Petrescu, M. (1940)

Bull. Off. int. Hyg. publ., **32**, 300.

Derrick, E. H. (1937) *Med. J. Aust.*, **2**, 281.

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Durand, P., and Giroud, P. (1940) *C. R. Acad. Sci., Paris*, **210**, 493.

Murgatroyd, F. (1940) *Trans. R. Soc. trop. Med. Hyg.*, **34**, 1.

UMBILICUS DISEASES

See Surveys and Abstracts 1940, p. 572.

1561-1569

UNDULANT FEVER (*MELITENSIS* AND *SUIS* TYPES)

See Surveys and Abstracts 1939, p. 584; 1940, p. 573; 1941-2, p. 416.

1571

URAEMIA

See Surveys and Abstracts 1941-2, p. 417.

1572

URETHRA DISEASES

See Surveys and Abstracts 1939, pp. 156 and 584; 1940, p. 574; 1941-2, p. 417.

1573, 1574

URINE EXAMINATION

See Surveys and Abstracts 1939, p. 585; 1940, p. 575; 1941-2, p. 418.

1575

UROGENITAL ORGANS, ABNORMALITIES

See Surveys and Abstracts 1939, p. 586; 1940, p. 576; 1941-2, p. 418.

1576-1578

UTERUS, DISEASES AND DISORDERS: I.—DEVELOPMENTAL ABNORMALITIES

See Surveys and Abstracts 1939, p. 587; 1940, p. 577.

1580

UTERUS, DISEASES AND DISORDERS: IV.—TUMOURS

See Surveys and Abstracts 1939, p. 588; 1940, p. 577; 1941-2, p. 419.

1586-1590

UVEAL TRACT DISEASES

See Surveys and Abstracts 1939, p. 590; 1940, p. 579; 1941-2, p. 420.

1591-1594

VACCINIA AND VACCINATION

See Surveys and Abstracts 1939, p. 590; 1940, p. 579.

1595

VEIN DISEASES

See also Surveys and Abstracts 1939, p. 591; 1940, pp. 13, 137, and 580; 1941-2, p. 420.

PHLEBITIS**Thrombophlebitis***Aetiology*

I. S. Wright, on the basis of more than 300 cases seen during the last 6 years, discusses the present confused views held about thrombophlebitis and its allied syndromes. It is not generally realized by the medical profession that there may be one, several, or many different diseases included under this heading. Of the last 70,000 patients in the New York Postgraduate Hospital, 182, or 0.26 per cent, were the subject of thrombophlebitis. In surgical cases the incidence is from 1.5 to 4 per cent. Among 274 cases analysed the causes recognized were: infection 63; varicose veins 51; trauma (a) injury 40, (b) post-operative 52; and unknown 59. Consideration of the classifications clearly showed that there are probably numerous distinct syndromes with individual characteristics as regards causation, physical background, course, and probable prognosis. In some of these syndromes the aetiological factors are quite clear, as in chemical and suppurative phlebitis; in chemical phlebitis the chemical irritation of the intima and other parts of the vein wall causes roughness of the intima and often spasm of the vessel, resulting in stasis with thrombosis, but without any evidence of primary bacterial invasion. There does not appear to be any micro-organism specific, or indeed predominantly numerous, in phlebitis. Attention is directed to the incidence of the relation of epidermophytosis to single and recurrent phlebitis of the feet and legs; this has suggested that the fungous infection may be responsible either directly or by an allergic response; the author and W. Dunham found that cultures of 15 of such veins were always negative, and that the whole picture is unlike an allergic reaction, and that it is more probable that bacteria, sub-bacterial forms, or viruses are admitted through cracks in the skin, produced by the fungus, and track upwards along the veins or lymphatics; this has not been yet proved. All the layers of the veins are usually inflamed and the perivenous lymphatics are involved, so causing oedema (J. Homans). As a sequel attention is directed to a post phlebitic neurosis chiefly seen in nervous women.

1596

Treatment

Treatment is described as being in a state of relative chaos, overwhelmed by the number of conflicting methods. Three forms are discussed. (1) *Prevention*: This includes the post-operative routine of the application of heat; early movement of muscles, but not to the excess of walking from the operating theatre after laparotomy; avoidance of dehydration and of tight bandages which favour stasis and thrombosis; cure of epidermophytosis of the lower extremities and of any disease of the blood-forming organs. The proper position of the thrombosed limb was formerly elevation; the opinion of Virchow and Aschoff that the commonest site of the origin of thrombosis was the femoral vein and its valve pockets has been contested by R. Frykholm, in favour of the veins of the calf and adductor muscles.

The results of the raised position of the limb are collapse of the veins and injury to the intima. Logically therefore the usually employed elevation of the limbs is the worst possible position, and he recommends, for both prevention and cure, that for 1 to 2 hours daily the head of the patient's bed be raised 18 inches, thus filling the veins. In persistent, recurrent, and migratory thrombophlebitis abstinence from tobacco seems to be important; in thromboangitis approximately 40 per cent of the patients suffer from thrombophlebitis. (2) *Conservative treatment*: The question of heat or cold applications has raised much controversy; recently local heat has been the more popular, and there are good reasons for this, but the author has seen numerous cases in which heat did not do any good, and a change to a cold application, such as an ice-bag, at once brought about improvement. Probably the greatest source of disagreement is between those advocating immobilization in bed with only mild movements and those in favour of compression bandages with unrestricted activity. For most patients, rest in bed with the leg elevated is the best; the policy of lowering the leg several times a day is prophylactic rather than curative. The use for 2 years of sulphanilamide, sulphapyridine, and sulphathiazole has given encouraging clinical results, but they have sometimes failed. In a small series of cases heparin appeared to speed up clinical improvement. The use of leeches has not been beneficial in the author's hands, and hirudin, the active principle of leeches, was disappointing. (3) *The radical or operative treatment*: Ligature of the vein well above the lesion has been employed to prevent both extension and pulmonary embolism, but it is not a certain preventive. The block of sympathetic ganglion by procaine hydrochloride is based on the fact that vasospasm is often one of the most important factors in the production of pain and disturbance of the venous circulation.

- Frykholm, R. (1940) *Surg. Gynec. Obstet.*, 71, 307.
- Homans, J. (1939) *Circulatory Diseases of the Extremities*, New York.
- Wright, I. S. (1941) *Bull. N.Y. Acad. Med.*, 17, 348.

VERTIGO

1598 See Surveys and Abstracts 1939, p. 593; 1940, p. 583; 1941-2, p. 422.

VITAMINS

See also Surveys and Abstracts 1939, p. 594; 1940, pp. 16, 31, 56, 70, 114, 117, and 585; 1941-2, pp. 5, 49, 120 and 422.

WATER-SOLUBLE VITAMINS

Vitamin B₁ and Beri-Beri

1602 The use of vitamin B₁ in the treatment of various forms of neuritis is discussed under the title Neuritis, on p. 225.

Symptoms of Overdosage

Steinberg has reported that, among over 300 patients treated with large doses of various preparations of the vitamin B complex or vitamin B₁ for chronic arthritis, herpes zoster occurred in 3 cases and symptoms suggesting spasm of smooth muscle in 2 others. The dosages in the 3 patients developing herpes zoster were as follows: (i) 800 units of vitamin B₁ orally and 2,000 units intravenously at weekly intervals; after 4 weeks typical herpes zoster lesions were present on the arm and chest; (ii) 2,000 international units intravenously at weekly intervals, and 800 units daily by mouth; after 5 weeks herpes zoster developed on the arm and chest; (iii) 1,200 international units of vitamin B₁ daily by mouth; after 2 months herpes zoster developed on the right upper elbow. The lesions in all cases disappeared 3 to 8 weeks after cessation of treatment. One patient after 6 months' massive treatment noticed a sense of fullness in the epigastrium, and a feeling of constriction of the throat within 2 minutes after an intravenous injection. Another felt constriction in the throat and severe cramps after several months of treatment. Steinberg considers that these two cases suggest either the development of sensitivity to vitamin B₁ or supersaturation of the tissues.

Vitamin B₂ Complex and the Pellagra-Preventing (P-P) Factor

Other Components of B₂ Complex

A review of most recent work on the vitamin B complex has been given by Meiklejohn. Evidence of riboflavin deficiency occurring in men has now been obtained (Sebrell). Of 18 women receiving over a long period a diet similar to that normally associated with pellagra, 13 developed lesions on the face: angular stomatitis and denudation of the mucous membranes of the lips and a scaly desquamation in the nasolabial folds and elsewhere. These lesions responded to administration of synthetic riboflavin but not to nicotinic acid.

Assessment of Level of Nutrition in P-P Factor

B. Naganna, K. V. Giri, and P. Venkatesam, using the method of L. J. Harris and W. D. Raymond, have confirmed that the urinary excretion of nicotinic acid by patients with pellagra falls to zero and rises to normal levels with cure. As was pointed out by the latter workers, the more precise method of assessing the reserves

of nicotinic acid is, however, to administer test doses as is done with tests for other vitamins and so determine the degree of saturation—that is, the number of days before a surplus is excreted at a constant rate in the urine. In the case of nicotinic acid the method is somewhat complicated by the fact that a large proportion of the nicotinic acid (or amide) ingested is excreted as trigonelline, which is itself biologically inert. Thus trigonelline may be derived not only from nicotinic acid but from trigonelline, which is present in certain foods. In an important paper E. Kodicek and Y. L. Wang describe a new method for the estimation of trigonelline. In the test-dose procedure which they recommend the patient is kept on a diet free from trigonelline, doses of nicotinic acid amide are administered, and the urinary excretion of both nicotinic acid and of trigonelline is estimated. Under these conditions the amount of trigonelline derived from inactive materials in the diet is negligible and the excretion of nicotinic acid and of trigonelline gives an index of the level of nutrition. In the absence of the controlled, trigonelline-free diet and of test doses, on the other hand, a more satisfactory indication may be obtained from the excretion of nicotinic acid itself.

FAT-SOLUBLE VITAMINS

Dihydrotachysterol (A.T. 10)

Dihydrotachysterol is a dihydro derivative of tachysterol, which is an isomer of ergosterol produced by irradiation of ergosterol. It is claimed that this substance raises the serum calcium to normal and relieves tetany in hypoparathyroidism. MacBryde found that 6 women suffering from chronic hypoparathyroidism (of 3½ to 17 years' duration), and one with idiopathic tetany, were completely relieved of their symptoms by doses of 0.3 to 1.0 c.cm. daily, supplemented by calcium lactate or gluconate 4 to 10 g. daily.

Hurxthal and Claiborne treated 6 patients with post-operative tetany of at least 2 years' duration with dihydrotachysterol. They found that 2 to 5 c.cm. weekly controlled the milder cases, but that larger doses were required in more severe cases. It is advisable to give calcium orally in addition, preferably calcium lactate.

Jacobi and Tigges tested the effect of dihydrotachysterol in 8 patients with various disorders. In one with tetany and hypocalcaemia which followed removal of a goitre the symptoms were relieved. In a case of sprue with severe hypocalcaemia the serum calcium was restored to normal with relatively small doses. In a case of idiopathic tetany with normal blood calcium the symptoms were cured. In another patient with idiopathic tetany and hypocalcaemia small doses were effective. On the other hand, treatment was unsuccessful in the following: a patient with excretory pancreatic insufficiency, colitis, and megacolon together with signs of tetany and hypocalcaemia; a child with nephrosis and hypocalcaemia without tetany, and a case of osteitis fibrosa cystica. One woman tolerated unusually large doses for 2 years, but showed no rise in the blood calcium.

OTHER VITAMINS

Vitamin K

The clinical use of vitamin K in the treatment of bleeding associated with obstructive jaundice is described on p. 168.

The position in the year 1940 with regard to vitamin K was discussed by Meiklejohn. It has now been isolated by several workers (Almquist and Klose; Dam *et al.*; McKee *et al.*), and vitamin K₁ (the form obtained from alfalfa) has been synthesized (Binkley *et al.*; Fieser *et al.*). It appears that several related compounds, all related chemically to naphthoquinone, possess vitamin K activity.

Vitamin K is believed to be essential for the normal synthesis of prothrombin and may actually be the active component of prothrombin. The presence of bile salts in the intestinal tract is essential for absorption of the vitamin, and any condition leading to deficiency of bile (e.g. chronic diarrhoea, intestinal obstruction, and surgical short circuits) may lead to deficiency of prothrombin in the blood. The vitamin appears to be produced by various bacteria, including the normal inhabitants of the intestinal canal. It is suggested that abnormalities in the intestinal flora in the newborn may partly account for deficiency of prothrombin leading to haemorrhagic conditions in the newborn.

Almquist, H. J., and Klose, A. A. (1939) *J. Amer. chem. Soc.*, **61**, 1611.

— (1939) *ibid.*, **61**, 1923.

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Fieser, L. F., Campbell, W. P., Fry, E. M., and Gates, M. D., Jun. (1939) *J. Amer. chem. Soc.*, **61**, 2559.

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Jacobi, J., and Tigges, F. (1939) *Dtsch. Arch. klin. Med.*, **183**, 558.
Kodicek, E., and Wang, Y. L. (1941) *Nature, Lond.*, **148**, 23.
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VULVA AND VAGINA DISEASES

- 1610-1612 See Surveys and Abstracts 1939, p. 600; 1940, p. 592; 1941-2, p. 429.

WHOOPING-COUGH

- 1613 See Surveys and Abstracts 1939, p. 601; 1940, p. 594; 1941-2, pp. 68 and 431.

YAWS

- 1615 See Surveys and Abstracts 1939, p. 604.

YELLOW FEVER

- See also Surveys and Abstracts 1939, pp. 145 and 604; 1940, p. 595; 1941-2, pp. 99 and 432.

FORMS AND THEIR GEOGRAPHICAL DISTRIBUTION

- 1616 The present position in South America is that there appear to be three forms of yellow fever: (1) and (2), aegypti transmitted urban and rural, and (3) the non-aegypti transmitted jungle type. The first two forms are acquired indoors and affect non-immunes of all ages in the vicinity, and on the whole tend to spread along the routes of human travel. There is close association of man with *Aedes aegypti*. The first two are readily controlled by anti-aegypti measures, but the jungle form can be brought under control solely by immunization of exposed members of the population. In the clinical, pathological, and immunological sense these various forms of the disease are indistinguishable. In Africa it appears now that the position resembles that of South America. The infected towns—Freetown, Lagos, Port Harcourt, Calabar, and other cities—were efficiently sanitized, and severe urban and rural outbreaks controlled, but these measures did not prevent outbreaks in other remote stations. The introduction of the mouse protection test showed that yellow fever extended from the coast to the Anglo-Egyptian Sudan, to Uganda and Abyssinia in the east, and from the Sahara in the north to Angola and the Belgian Congo in the south, but in very large tracts of this huge area no clinically recognizable case of yellow fever has been recorded. A possible explanation of the endemicity of jungle yellow fever in South America and Central Africa may lie in a monkey reservoir of the virus. The red-howler monkey (*Myetes seniculus*) was recorded by A. Balfour as dying of yellow fever in Trinidad and Venezuela, and L. van den Berghe has found that the blood serum of *Colobus polykomos* in Central Africa gives a positive mouse protection test.

EPIDEMIOLOGY AND IMMUNITY

Outbreak in Nuba Mountains

In October 1940 the most extensive epidemic of yellow fever ever recorded in Africa broke out in the Nuba Mountains, where previously a case of the disease had not been observed clinically, although serum tests taken in 1934 had indicated that the virus did in fact exist in this district. The outbreak involved an area of 6,000 square miles with 18,000 recognizable cases, and 1,800 deaths. The epidemic lasted for two months before it was brought under control by mass immunization with the yellow fever vaccine.

VIRUS AND VECTORS

Mosquitoes acting as vectors.—*Aedes geniculatus* has been found by Callot in the Department of Indre-et-Loire and in different parts of Alsace and in Seine-et-Oise. It breeds in rock-holes in which there is water containing rotting vegetable matter. This species has been found to be an efficient vector of yellow fever.

Roubaud *et al.* have shown that *Aedes geniculatus* can transmit yellow fever by its bite if kept at 30 to 35° C.; but when these insects were fed on blood containing yellow fever virus and, after 5 days at 30° C., kept at 20 to 22° C., and then fed on a normal monkey, they produced neither infection nor immunity.

PATHOLOGY AND MORBID ANATOMY

The Councilman-Rocha-Lima cell.—Montenegro once more defines the typical Councilman cell in the yellow fever liver. Tissue stained with haematoxylin and eosin shows coagulative necrosis with a well-marked edge surrounded by a narrow clear halo; the cytoplasm is eosinophilic, non-granular, more refractile than normal,

and contains small vacuoles; the nucleus is smaller and more rounded than that of the normal cell.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Mouse-protection test.—The Yellow Fever Commission does not recommend the mouse-protection test for the diagnosis of yellow fever in doubtful febrile diseases with clinical signs of yellow fever. It is only of real value for making a retrospective diagnosis in a community suffering from an epidemic of uncertain nature.

TREATMENT

Precautions against aerial transport of disease.—The destruction of mosquitoes in aircraft whilst in flight would obviate the practical difficulties of providing insect-free aerodromes. The choice of an insecticide presents difficulties as it is essential that it should exert no effect on passengers or crew; and, in view of the risk of fire, any substances with a paraffin-base have to be avoided. Mackie and Crabtree found that the most satisfactory was deskito, a pyrethrum insecticide in a watery base, distributed through the interior of the aircraft by a spray apparatus. Two types of spray were used—a disseminator to distribute 'dry' insecticide to the passenger cabins and an 'ejector' suitable for luggage holds, bedding lockers, and all other parts of the aircraft. The 'phantomyst nebuliser' was used for passenger cabins and Larmuth's device, driven by pressure of carbon dioxide in a sparklet bulb, for the ejector type.

The results of various experiments carried out for Imperial Airways have shown the efficacy of this method.

This subject is also discussed by Ross and by Cumming.

Prophylactic inoculation.—With regard to the use of prophylactic vaccination against jungle fever, mass vaccination is now recommended.

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